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Title of Dissertation: "Application of Solid Phase Microextraction with Gas Chromatography-Mass Spectrometry as a Rapid, Reliable, and Safe Method for Field Sampling and Analysis of Chemical Warfare Agent Precursors"

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## **ABSTRACT**

Title of Dissertation: “Application of Solid Phase Microextraction with Gas Chromatography-Mass Spectrometry as a Rapid, Reliable, and Safe Method for Field Sampling and Analysis of Chemical Warfare Agent Precursors”

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Solid phase microextraction was combined with gas chromatography-mass spectrometry (SPME-GC-MS) for detection of hydrogen cyanide (HCN) in the headspace above deionized (DI) water samples, with linear results that were sensitive to below Department of Defense short-term drinking water standards. HCN and several common volatile organic contaminants were also detected in 3 water types in a laboratory and field setting. The method provides an advantage over the standard drinking water detection methods for HCN as it can also simultaneously detect common low molecular weight hydrocarbons.

Linear results were achieved for the detection of diisopropylamine (DIPA) by SPME-GC-MS in soil from 0.72 - 3584.5  $\mu\text{g}$  DIPA/g soil and in DI water from 0.018 - 17.9  $\mu\text{g/mL}$ . The methods were successfully field tested with common hydrocarbon contaminants in 3 common agricultural soil types and 3 water types. In particular, this methodology would be useful for investigation of a suspected VX nerve agent production facility.

Solid phase dynamic extraction (SPDE) was compared to passive SPME for vapor sampling of DIPA and dimethyl methylphosphonate (DMMP) with analysis by fast GC-MS. Equilibrium sampling by SPDE for DIPA and DMMP vapor provided linear results at lower concentrations and gave larger extracted ion peak areas than comparable SPME sampling. This unique application has shown great potential for further laboratory and field use, both for health risk assessment and initial chemical detection employment.

A fast GC capillary column was integrated with a novel low pressure, quadrupole ion trap, time-of-flight photoionization mass spectrometer (Qit ToF PI-MS). The addition of a GC injection port and column allowed the use of SPME to provide headspace extraction of several chemical warfare agent (CWA) precursors for introduction to this GC/PI-MS. This prototype instrumentation was shown to be able to detect CWA precursor vapors in air individually and in mixtures.

The central research goal was to develop the ability to rapidly detect CWA precursors in a field setting. The greatest benefit to using these SPME-GC-MS methods is they allow unambiguous detection and identification of CWA precursors as well as common environmental contaminants. These detection methods are applicable to the military environmental scientist as well as homeland defense and hazardous material

detection personnel. Identification of environmental chemicals is the first step in assessing military deployment exposures and health risks.

APPLICATION OF SOLID PHASE MICROEXTRACTION WITH GAS  
CHROMATOGRAPHY-MASS SPECTROMETRY AS A RAPID, RELIABLE, AND  
SAFE METHOD FOR FIELD SAMPLING AND ANALYSIS OF CHEMICAL  
WARFARE AGENT PRECURSORS

by

LT Douglas K. Parrish, MSC USN

Dissertation submitted to the Faculty of the Department of Preventive Medicine and Biometrics, Graduate Program of the Uniformed Services University of the Health Sciences, in partial fulfillment of the requirement for the degree of Doctor of Philosophy in Environmental Health Sciences, 2005.

## DEDICATION

To my wife, Jennifer, and my children, Ellie and Roan, for the sacrifices you made during my Navy career and the last 3 years of study. I dedicate this dissertation to you.

To the other women in my life: my mother, Gayle, and grandmothers, Mae Belle and Martha, thank you for your love, support, and encouragement over the years.

In loving memory of my father, Jim, and grandfather, James A: your love of knowledge and books gave me great inspiration over the years.



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# CHAPTER 1

## INTRODUCTION

### Research Question and Specific Aims

**I. Research Question:** Can solid phase microextraction (SPME) coupled with gas chromatography-mass spectrometry (GC-MS) provide a rapid, reliable, and safe method for field sampling and analysis of chemical warfare agent precursors?

### II. Specific Aims:

1. Develop a method to quantitatively detect hydrogen cyanide in the headspace above cyanide-contaminated water.
2. Develop a method to quantitatively detect diisopropylamine in the headspace above water and soil samples.
3. Develop and explore a novel methodology based on needle-trap solid phase microextraction to quantitatively detect dimethyl methylphosphonate and diisopropylamine in air.
4. Develop a qualitative method using solid phase microextraction to concentrate samples of precursors for identification with a novel Syagen photoionization mass spectral detector via a fast gas chromatograph.



## **CHAPTER 2**

### **LITERATURE REVIEW**

#### **I. BACKGROUND AND SIGNIFICANCE**

The use and presence of chemical warfare agents (CWAs) are of ongoing concern in both the military and civilian world [1]. The “1994 Convention on the Prohibition of the Development, Production, Stockpiling, and Use of Chemical Weapons and Their Destruction” forbids the use of riot control agents like CS in warfare. However, U.S. troops and police personnel can reasonably expect to see these irritants as well as more harmful chemical warfare agents abroad during both wars and peacekeeping missions. They may also be encountered at home in civil support taskings, both from hostile action and inadvertent environmental release [2]. The use of CWAs by terrorists against U.S. assets either at home or overseas is a current and potentially growing threat. The Department of Defense has an urgent requirement to develop rapid sampling and detection protocols related to CWAs including precursors, degradants, and the neat agents themselves, that will provide unambiguous identification in the field for both military (threat detection) and medical reasons (health risk assessment).

Hydrogen cyanide (HCN) is a common chemical that poses both a toxic industrial chemical (TIC) concern as well as a threat from overt or covert terrorist and wartime use. HCN is a precursor and hydrolysis decomposition product of the nerve agent Tabun and is also a common industrial chemical feedstock [1,3-5]. Diisopropylamine (DIPA) is an intermediate precursor for the nerve agent O-ethyl S-(2-diisopropylaminoethyl)

methylphosphonothiolate (VX), and certain pesticides, and is a chlorination decontamination product of VX [1,3,6]. Dimethyl methylphosphonate (DMMP), used commercially in organic synthesis, is an intermediate precursor for Tabun, Sarin, and Soman [1,4,7]. Table 2-1 provides characterization and data regarding Organisation for the Prohibition of Chemical Weapons (OPCW) regulation of these chemicals. Greater details on specific industrial uses and toxicology are discussed for each chemical in Chemical Characteristics and Properties, Section II.

**Table 2-1. Selected Chemical Warfare Agent Precursors**

<b>Chemical Name</b>	<b>OPCW schedule [3] (Note)</b>	<b>Precursor for [3,4]:</b>	<b>Characterized as [4]:</b>
Hydrogen cyanide	3A	Tabun	Dual threat
Diisopropylamine	*	VX	Dual threat
Dimethyl methylphosphonate	2B	VX, G agents	Dual threat

**NOTE:** The OPCW has the following management schedules [3]:

Schedule 1, known CWA.

Schedule 2A, toxic chemical or direct threat.

Schedule 2B, direct precursor to a CWA.

Schedule 3A, toxic chemical or direct threat, less than 2A.

Schedule 3B, intermediate precursor for a CWA.

\*Not scheduled but on the OPCW precursor list.

#### *Detection methods in the field and laboratory*

There are a number of different collection and detection systems used both in the laboratory and field environment for CWA monitoring. One-dimensional sensors or presumptive detection methods are the simplest in terms of technology and use. These instruments are generally the most susceptible to interferences and false positive identification. The earliest designs were based on colorimetric paper and wet chemistry.

More advanced one-dimensional systems employ such principles as surface acoustical wave (SAW) sensors based on electromechanical response, electrochemical sensors based on the amperometric response of an enzyme biosensor, flame and photoionization devices based on ionization potential, spectrophotometric sensors based on color spot tests, sorbent tubes that show a chemical-induced color change, and immunochemical sensors based on fluorescence, electrochemical response, or enzyme-linked immunoabsorbent assays [8].

Two-dimensional (2D) or intermediate sensors are more capable of separating individual chemicals from a matrix or mix of chemicals and interferents. Common 2D devices include liquid or gas chromatography (LC or GC), capillary electrophoresis (CE), ion mobility spectrometry (IMS), infrared (IR) and Fourier Transform Infrared (FTIR) spectrometry, and mass spectrometry (MS) [8].

Three-dimensional (3D) or advanced detection sensors give more accurate chemical identification but are often difficult to transport to the field due to their physical size and because of complexity restrictions. Examples of orthogonal, 3D systems include hyphenated systems such as GC-MS, LC-MS, IMS-MS, and CE-MS. Four-dimensional (4D) sensors include GC-MS-MS and GC-IMS-MS and provide greater detail for the identification of similar chemicals [8]. These advanced systems generally require much more training to master as compared to 1D and 2D systems.

There are multiple methods to extract chemicals from air or the headspace above a sample and prepare them for analysis with a GC-MS. Traditional sampling on a sorbent media often requires the use of liquid solvents to extract analytes from the sorbent media used for collection and for dilution of highly concentrated samples. These methods

potentially produce a large waste stream of toxic chemicals. To reduce the need for solvents, air samples can be collected in a gas-tight syringe and directly injected into the analytical instrument. This method can be problematic when the analyte is at trace levels in the sample as the sampling step does not concentrate the analyte [9].

Solid phase extraction is a method that concentrates the analytes during sampling and eliminates some sample preparation steps. Similarly, use of solid phase microextraction (SPME) presents a powerful method that lends itself to characterization of a wide variety of chemicals in various media and through a wide range of concentrations, especially when paired with GC-MS analysis [9]. Additional information on SPME is discussed in Chapter 2, Section IIIA.

The use of GC-MS has been well characterized for CWA identification but not for identification of most CWA precursors [10-12]. The limited data available specifically for the identification of selected CWA precursors are discussed in Chapter 2, Section IIA. GC-MS instruments are considered by many to be the “gold standard” for CWA and toxic industrial chemical (TIC) identification because a GC-MS can provide detailed information about a chemical’s structure. With a GC-MS, it is possible to identify many known and unknown chemicals in a variety of matrices equating to the ability to correctly identify precursors, CWAs, and common organic compounds in the same sample. The quantitation of chemicals in environmental samples requires additional sampling and analysis. Further information on GC-MS is provided in Chapter 2, Section IIIC.

Several authors have supported the concept of a field portable GC-MS and specific, field-ready sampling techniques including the use of SPME [13-15]. Previous graduate students in the Environmental Health Sciences (PhD and MSPH) programs at

the Uniformed Services University of the Health Sciences (USUHS) have performed relevant chemical warfare and TICS analyses [16-18]. The work and methodologies completed at the USUHS Environmental Chemistry Laboratory are particularly suited to increasing military and homeland defense readiness. The USUHS graduate and faculty work in chemical warfare agent and precursor detection methods have been used by military forces, including the United States Marine Corps (USMC) Chemical Biological Incident Response Force (CBIRF), Indian Head, MD. CBIRF is charged with incident response and consequence management in the national capitol region and around the world and has had ample opportunity to evaluate the USUHS methods in the field. The particular methods developed by Smith, Hook, Kimm, and others have been collected into a joint working document, the “USUHS/Defence Research and Development Canada (DRDC)/CBIRF Chemical Agent Detection Handbook” [19].

The ability to detect and positively identify CWA precursors can be extremely important in confirming that a site was involved in CWA manufacture as opposed to employment for standard industrial operations such as pesticide production. The focus of this research was on developing methods for precursor identification that would be applicable for fieldwork.

## **II. CHEMICAL CHARACTERISTICS AND PROPERTIES**

Acronyms used in this dissertation are listed in Appendix 1. Pertinent physiochemical characteristics for the chemicals of interest are listed in Appendix 2. The molecular structures are depicted in Appendix 3. A summary of acute toxicology data for each chemical is presented in Appendix 4.

## **II A. Hydrogen cyanide**

### *1.1 Background*

Hydrogen cyanide (HCN) is a widely used industrial chemical. U.S. demand in 2002 was 725,000 metric tons. Cyanide is used in numerous processes in industrial nations, including plating solutions, metallurgical processes such as silver and gold refining, and as an intermediate in the manufacture of resin monomers, methacrylates, and nitriles [5].

HCN exists as a gas or liquid, depending on the mixture. It will exist solely in the vapor state in the atmosphere based on its vapor pressure of 742 mm Hg at 25 °C and will be slowly degraded by reaction with photochemically-produced hydroxyl radicals and ozone (half-life of 535 days). Based on its water solubility and organic content constant ( $K_{oc}$ ), HCN is expected to have very high mobility in soil and to not adsorb to sediments in water. The Henry's Law constant of  $1.33 \times 10^{-4}$  atm-m<sup>3</sup>/mole indicates that it will readily partition from water to air as a vapor (theoretical half-life of 3 days in lakes, 3 hours in rivers) and may volatilize from dry soil [5].

There are many chemicals that may be present in drinking water as pollutants or intentional contaminants, including various cyanide salts such as KCN and NaCN. Water supplies, production facilities, distribution systems, and storage facilities are all potentially susceptible to inadvertent or intentional cyanide contamination, which can pose a health risk to civilian and military populations.

Cyanide is still widely used to stun fish in Third World salt- and fresh waters by poisoning as a method of gathering the fish for eating and for tropical aquarium suppliers [20]. Large environmental releases of cyanide occurred in 1999, resulting in the release

of HCN gas as a byproduct of fires on top of settling ponds associated with phosphorus mining [21]. HCN is a precursor and primary hydrolysis product of Tabun (ethyl N,N-dimethylphosphoro-amidocyanide) [1]. Most modern purposeful widespread exposures to cyanide have been by air. It was used in World War I artillery, as Zyklon B in World War II death camps, in two separate unsuccessful terrorist incidences in Tokyo subways in 1995, and possibly for the gassing of Kurds in Iraq in the 1980's [22-24]. Other than individual and small group poisonings by cyanide-laced beverages, public water supplies in the U.S. have not yet been purposefully attacked [24]. However, the potential for intentional and unidentified contamination should not be discounted.

### *1.2 Cyanide Health Effects*

Only extremely high order toxicants such as VX exceed cyanide's acute toxicity by more than one order of magnitude. Cyanide is fairly easily found, prepared and disseminated, especially for water delivery [24]. KCN, CaCN, and NaCN are common cyanide salts that disassociate in water, evolving into HCN upon contact with air. Cyanide poisoning by ingestion, inhalation, or dermal exposure occurs quite rapidly by virtue of interference with cell respiration [24]. Chronic effects in workers include central nervous system effects, thyroid enlargement, and hematological disorders [25,26]. A comparison of cyanide to CWAs is presented in Appendix 5.

For public water supplies, the United States Environmental Protection Agency (EPA) maximum concentration level for cyanide in drinking water is 0.2 ppm (0.2 mg/L) [27]. HCN is on the EPA Extremely Hazardous Substances List [28] and is an EPA-regulated Hazardous Air Pollutant [29]. The OSHA air standard for employee exposure

to HCN in the air is a Short Term Exposure Limit (STEL) of 4.6 ppm (5 mg/m<sup>3</sup>), and Immediately Dangerous to Life and Health (IDLH) limit of 50 ppm (56 mg/m<sup>3</sup>). OSHA has assigned HCN a “skin” designation, indicating potentially high levels of absorption via the skin [5].

## **II B. Diisopropylamine**

### *1.1 Background*

Diisopropylamine (N-(1-methylethyl)-2-propanamine or DIPA) is produced by reaction of ammonia with isopropyl alcohol or isopropyl chloride. DIPA is a chlorination decontamination product of VX [1]. DIPA is used as a chemical intermediate in the synthesis of pesticides (diallate and fenamiphos), chemical warfare agents (VX), and pharmaceuticals (preparation of vitamin B-15 and anti-hypertensives), with an estimated U.S. annual production of over 450 metric tons. DIPA is also used as a medication and as a stabilizer for mesityl oxide [6].

DIPA exists solely as a vapor in air due to its vapor pressure of 79.4 mm Hg. In the atmosphere, DIPA rapidly degrades by photochemically-produced hydroxyl radicals (estimated half-life of 4 hours). DIPA can exist as a neutral or positively charged compound with the neutral units not adsorbing to soil or sediments and the cations being dominant and somewhat adsorbing to both moist soil and sediment. In soil, DIPA is estimated to have a  $K_{oc}$  of 140 (derived from experimentally proven  $\log K_{ow}$  or octanol/water partition coefficient) and is expected to demonstrate high mobility for the neutral species. The vapor pressure and  $K_{oc}$  are high enough that DIPA is expected to



volatilize from dry soil. DIPA is not expected to readily volatilize from most moist soils (assuming neutral to mildly basic soil conditions), based on the high acid-base ionization constant ( $pK_a$  of 11.7). DIPA is most likely to exist in soil in the protonated form based on the  $pK_a$ , and thus will bind to organic content and colloidal clay in soils [6].

At >50 ppm, DIPA is theorized to be toxic to microbes in soil and water. Below that level, biodegradation is expected to be a major fate of DIPA in soil and water with acclimated microorganisms. The estimated bioconcentration factor (BCF, derived from the experimentally proven  $\log K_{ow}$ ) of 2 indicates low bioconcentration in marine life [7].

### *1.2 DIPA Health effects*

DIPA is an eye, respiratory and skin irritant. In humans, symptoms of DIPA exposure can range from nausea (low concentration) to pulmonary edema and burns (high concentration) [6]. OSHA has set a permissible exposure limit (PEL) for air of 5 ppm (20  $mg/m^3$ ), a skin designation, and 200 ppm (842  $mg/m^3$ ) IDLH limit [6]. No information was discovered showing that EPA regulates DIPA in the environment.

## **II C. Dimethyl methylphosphonate**

### *1.1 Background*

Dimethyl methylphosphonate (DMMP) is a common industrial solvent and additive, used in the manufacture of plastics and for heavy metal extraction as well as in the production of phosphorus-based nerve agents [4,8]. DMMP hydrolyzes to the half ester and methanol (13.2 year half-life at 20 °C). The half-life in water is temperature and concentration dependent (7 - 210 days in muddy water), but the exact removal

mechanisms such as volatilization, adsorption, hydrolysis, photolysis, or biodegradation from water are not known. DMMP is expected to hydrolyze in moist soils with a half-life of 0.2 - 60 days, and average of 12.4 days. Information was not available for volatilization or biodegradation rates, but the low vapor pressure (0.61 mm Hg at 25 °C) suggests it will have fairly low volatility [8]. DMMP is commonly used as a G-agent simulant.

### *1.2 DMMP Health effects*

DMMP has been shown to cause muscle weakness, respiration depression, and decreased fertility in rats, but there are no direct human health data [7]. EPA does not regulate DMMP but provides two Health Advisory levels for water consumption: Life-time exposure level of 100 ppb (0.1 mg/L) and a Drinking Water Equivalent Level of 7 ppm (7 mg/L) [26]. OSHA does not currently regulate DMMP exposure.

## **III. MATERIALS AND EQUIPMENT**

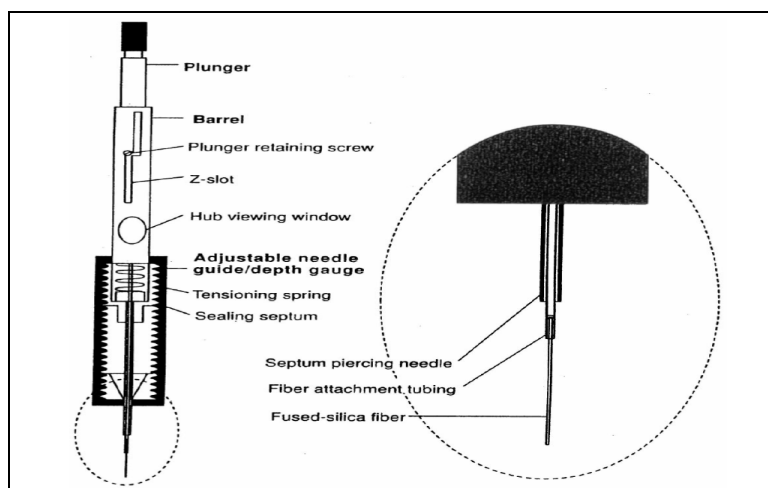
### **III A. Solid phase microextraction**

SPME is a generally simple, fast, and inexpensive sampling strategy that reduces or eliminates the use of solvents, eliminates cumbersome analytical steps, and reduces the analyst's exposure to potentially deadly chemicals [9]. The use of SPME can benefit the field analyst by reducing the logistical footprint required by a reduction in solvents and waste streams. Also, the use of SPME can increase sampling speed and ease sample concentration and introduction to the GC-MS. SPME is a fairly new research tool but has proven to have great potential for quick, accurate analysis in laboratory and field settings,

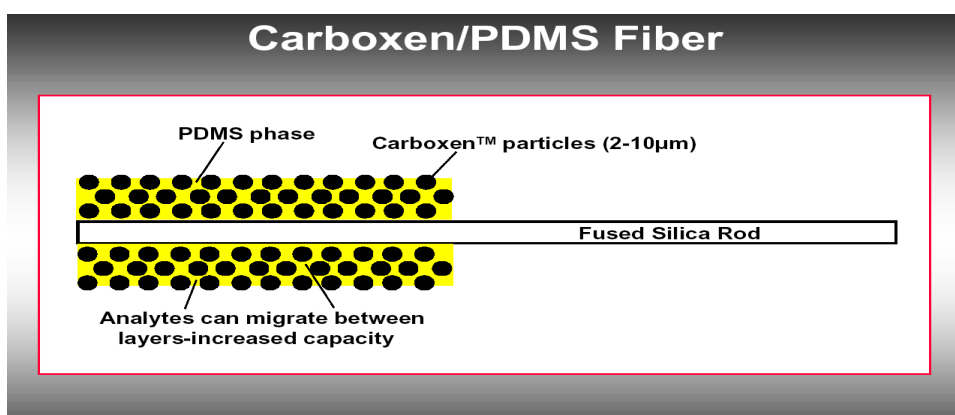
making it particularly useful to the military environmental scientist. Many portable and traditional benchtop GC instruments will accept the SPME fiber in a modified injection port liner (i.e. the liner is a different size and shape than used for liquid injections).

Originally employed for volatile organic compounds in environmental sampling, SPME use has since been expanded greatly into other areas including analysis of a wide range of analytes from volatile to nonvolatile compounds in numerous matrices (gas, liquid, and solid). The particular uses of SPME have previously been described in detail [29,30]. Different types of extraction devices can be coated with SPME polymer, including commercially available fibers, needletrap devices, stirbars, and in-tube sorption devices [9, 29,30].

SPME is basically a two-step process. Semi-selective chemical extraction and concentration are accomplished on a thin silica fiber coated with a stationary phase material, followed by desorption of the collected analytes in the heated GC inlet. This methodology virtually eliminates complicated sample preparation steps [9]. Figure 2-1 is a drawing of a SPME fiber and manual holder. Figure 2.2 shows a typical commercial fiber and coating.



**Figure 2-1.** SPME Fiber Sampler [31]



**Figure 2-2.** Typical Commercial SPME Fiber and Coating [32]

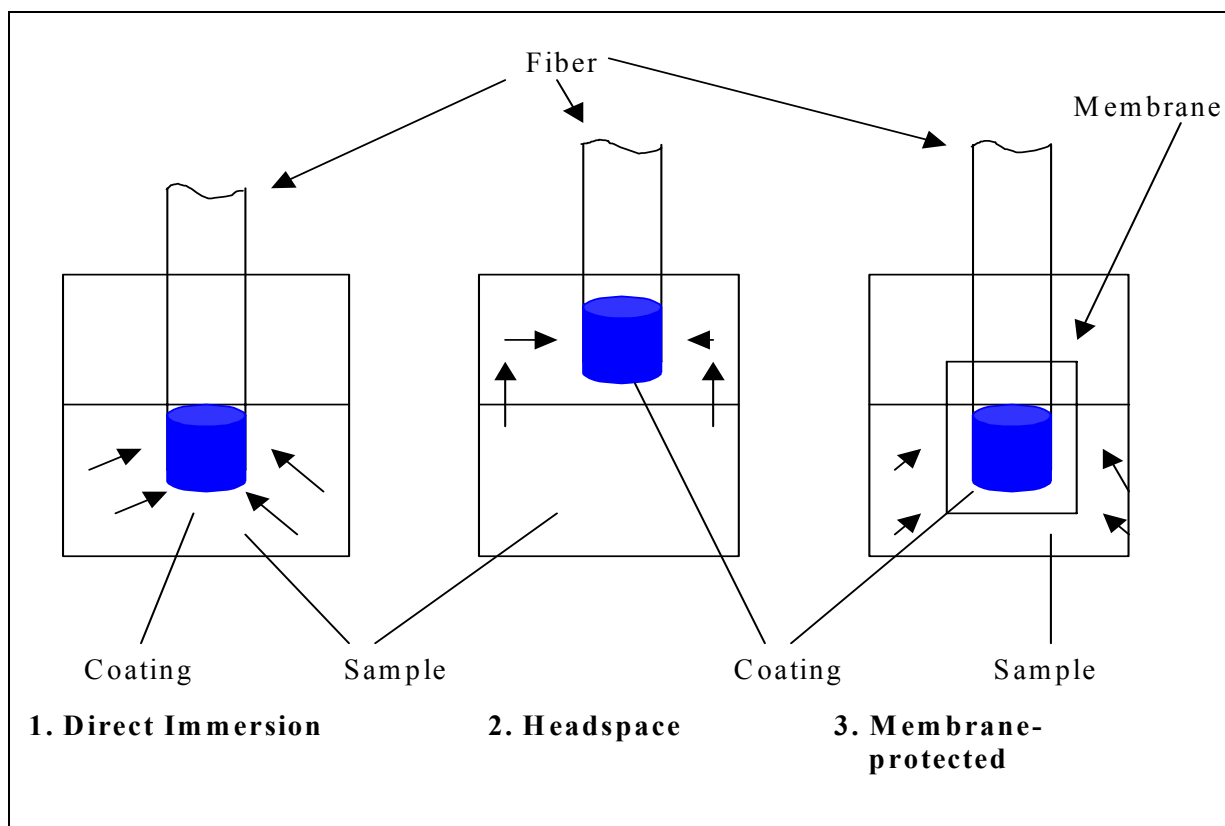
To protect the delicate SPME fiber from damage, it is equipped with a protective metal sheath for storage, transport, and piercing of septa (Figure 2-1). The selective extraction of the analytes of interest depends on the selection of the appropriate stationary phase coating. There are 6 common SPME fibers that are commercially available, each with particular characteristics that make it preferable for a specific sampling need though there is some overlap in specificity [9]. Table 2-2 shows types of commercial SPME

fibers by polarity. Generally, polar materials will best be sampled with a polar fiber and vice versa [30,33].

**Table 2-2.** Commercial SPME Fibers By Polarity [30]

Polarity	Name	Sizes ( $\mu\text{m}$ )
Nonpolar Fibers	1. Polydimethylsiloxane (PDMS)	100, 30, 7
Polar Fibers	1. Polyacrylate (PA)	85
	2. Carbowax-Divinylbenzene StableFlex (CW-DVB)	65
Bi-Polar Fibers	1. PDMS-DVB StableFlex	65
	2. Carboxen-PDMS StableFlex	75
	3. DVB-Carboxen-PDMS StableFlex	50/30

Direct, headspace, and membrane sampling are possible with SPME and are useful for sampling liquid and solid substrates [30,34]. Figure 2-3 shows how these methods are each employed. Headspace sampling describes a technique where chemicals are injected into a Tedlar bag or vial and allowed to evaporate or chemicals injected into water or soil, then heated or stirred to encourage them to partition into the headspace. Headspace sampling was employed exclusively during this research.



**Figure 2-3.** SPME Extraction Modes [adapted from Pawliszyn, 1997]. Arrows in the sample and headspace indicate travel paths of analyte molecules.

It is possible to sample with the SPME fiber until equilibrium has been reached between the fiber's coating and the analyte in the sample matrix and headspace [30]. Equilibrium time depends on the SPME polymer used, the physical state of the analyte, sample matrix, and other variables including temperature, pH, and characteristics of the chemical such as its Henry's Law constant, dissociation constants, and octanol-water constant [30,35]. The specific decay rates and loss of analytes from commercial SPME fiber coatings are well documented [33].

### III B. Solid phase dynamic extraction

Needle trap devices that employ solid phase microextraction were originally developed by Pawliszyn and others, and include use of a needle to protect a regular SPME fiber, use of a needle trap that is coated with a SPME polymer, and devices formed around a piece of chromatographic column [36-42]. The potential advantages of such a needle trap device over a typical SPME fiber would be greater mechanical durability of the phase since it is enclosed, greater phase volume, and hence greater sensitivity and increased extraction speed [38]. The ChromSys, Inc (Alexandria, VA) solid phase dynamic extraction (SPDE) needletrap devices (Figure 2-4) are slightly different than similar devices in that the SPME polymer is attached to the inside of a 0.8 mm needle instead of using a piece of chromatographic column [37-39]. ChromSys has a commercially available needle-trap device using SPME polymers, similar to but larger than the in-tube SPME micro-syringe developed by Supelco [37]. The SPDE has successfully been used in laboratories in an automated CombiPAL (Leap Technologies, Carrboro, NC) system for direct immersion and headspace sampling, but requires specialized sampling equipment, since the best results with automated SPDE devices require multiple extractions (by moving the plunger up and down in a sample multiple times) [38].



**Figure 2-4.** ChromSys Solid Phase Dynamic Extraction needletrap device. The inside of the stainless steel needle is coated with the polymer, PDMS-AC. A standard 6" ink pen is shown for scale.

Rasmussen et al. have employed hollow fiber-based liquid microextraction, similar to the SPDE but with a porous shell and liquid vice solid absorbent bed, for extraction of environmental pollutants and pharmaceutical products from liquid samples, with analysis by GC-MS and LC/MS [39]. Lipinski published the first paper on SPDE, employing automated sampling using the ChromSys SPDE device for organic compounds in water [38]. Others have used needletrap devices coated with SPME polymers for the concentration of organic vapors in air samples [40] as well as particulates in diesel engine exhaust [36]. Mushoff et al. have used SPDE for automated headspace sampling of drugs in hair samples with analysis by GC-MS [41,42].

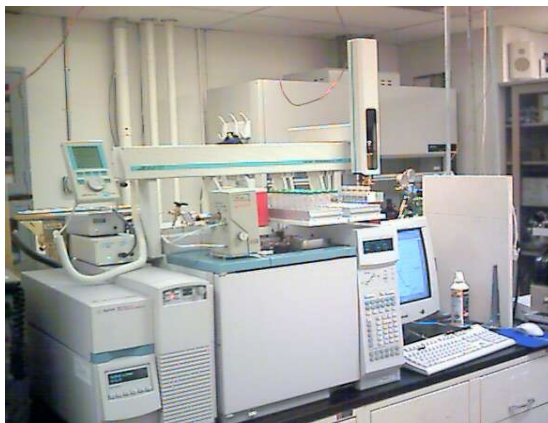
The research discussed here examined a polydimethylsiloxane polymer with 10% activated charcoal (PDMS-AC) solid phase dynamic extraction (SPDE) needletrap device for use with a small air sampling pump to determine its efficacy in extracting and concentrating several precursors individually in air samples without further sample preparation. Dynamic extraction has been proven to provide increased sensitivity, but requires the use of a special sampling block or chamber for commercial SPME fibers [43,44]. This research sought to expand the use of the SPDE and make it available for fieldwork on a standard GC-MS by coupling a SPDE needletrap device to a handheld air sampling pump. The use of a small pump obviated the need for automated or repeated plunger extractions or aspiration cycles. The results of sampling for a vapor by SPDE were compared to those produced when sampling with a standard SPME fiber. SPDE needle trap devices, if shown to have increased sensitivity for a wide range of chemicals as compared to commercial SPME fibers, may supplement or partially replace currently existing SPME fibers.



### **III C. Gas chromatograph-mass spectrometer**

A GC-MS is an orthogonal detection system that provides retention time, peak intensity, and mass spectral data. The GC column provides compound separation while the MS provides compound ionization and identification. By comparison with a mass spectral library and through the use of standards for retention time and spectrum matching and spectrum interpretation, unknown compounds can be identified with a high degree of accuracy. A generic GC-MS block diagram is included as Appendix 6. The uses of GC-MS for CWA detection are well described [10-12].

Analysis to detect each chemical was initially performed in a laboratory on a benchtop 6890 series gas chromatograph with a 5973 quadrupole mass selective detector (Agilent Technologies, Wilmington, DE) (Figure 2-5) or on a Viking 573 (Bruker Daltonics, Billerica, MA) (Figure 2-6) portable GC-MS. Fieldwork was accomplished on the USMC CBIRF Mobile Van, outfitted similarly to the laboratory GC-MS but without the autosampler, and employing hydrogen vice helium as the carrier gas. The Viking 573 was also used for fieldwork and was outfitted similarly to the CBIRF Mobile Van instrument but with helium carrier gas. Both the Viking 573 and CBIRF GC-MS devices were also later changed to accept a modified oven door and GC column to allow flash chromatographic separations. All of these instruments employ quadrupole electron impact mass spectrometry, a “hard” ionization method that breaks molecules down into descriptive ions.



**Figure 2-5.** Agilent 6890/5973 GC-MS with CombiPAL autosampler.



**Figure 2-6.** Viking GC-MS with fast GC door.

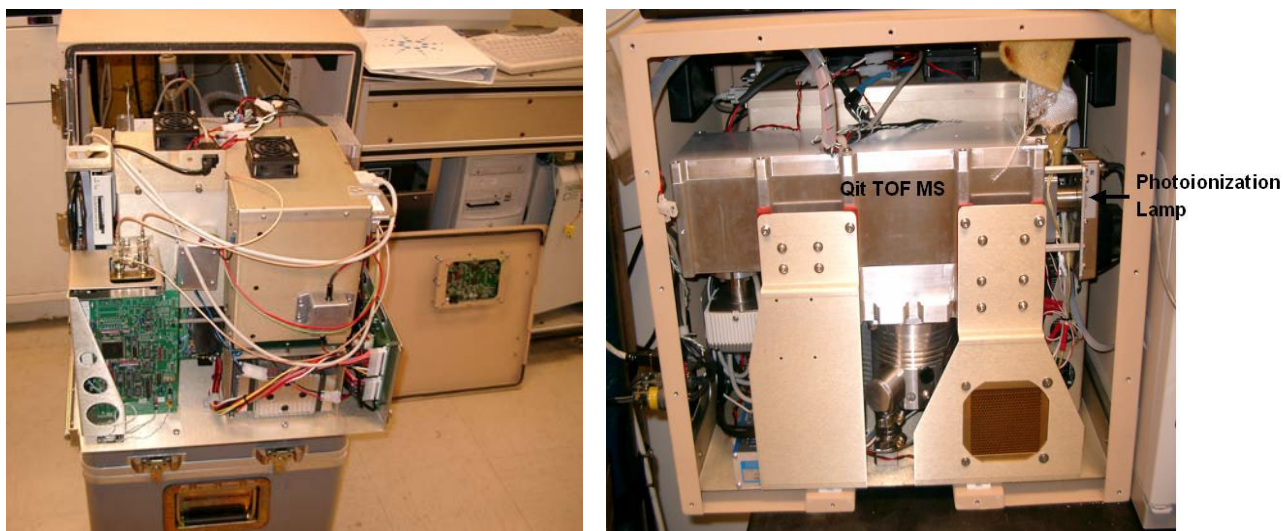
Similar to chemical ionization, photoionization (PI) is a soft ionization method that leaves a relatively intact parent ion, allowing ready identification of many high molecular weight chemicals. It has the additional benefit of minimal signal from air and most solvent molecules.

Borsdorf et al. have employed atmospheric pressure photoionization (APPI) coupled with MS-MS for detection of dihalogenated benzenes [45]. LC with APPI-MS

has been used for detection of antibiotic residues in fish [46]. APPI-MS has also been used for on-line, near-real time detection of gaseous and particulate organic analytes [47].

Syagen Technologies, Inc. (Tustin, CA), developed a novel photoionization source that allows sub-atmospheric and atmospheric pressure ionization, coupled with LC or MS detection. The company has several systems, including time of flight MS (TOF MS) and sample introduction by GC, pyrolysis, and other methods [48,49]. The company is developing a SPME-GC-MS system as well as a field portable unit based on APPI-MS [50]. DMMP and other precursors as well as CWAs have been detected using the Syagen PI-MS, coupled with a QitTof MS [50,51].

The Syagen low pressure photoionization (LPPI) source has been shown to produce low noise, a relatively low detection limit, and high specificity for the identification of CWAs by direct sampling (i.e., without the use of a chromatographic column). Additional benefits of use of this relatively new LPPI detection technology include increased sensitivity for the detection of CWAs as compared to many traditional systems [48-50]. The benefit of employing an atmospheric pressure system as compared to a traditional high vacuum system is the reduction in vacuum required, equating to a smaller, lighter, lower power requirement pump and instrument. The LPPI is between the two in terms of power and weight. The Syagen Inc. RadiancePro FieldMate<sup>TM</sup> PI-MS used for this research is shown in Figure 2-7.



**Figure 2-7.** Left, rear view (case off) of the Syagen Technology, Inc RadiancePro FieldMate™ Quadrupole Ion Trap Time of Flight Photoionization Mass Spectrometer. Right, front view of the FieldMate™.

The PI-MS is equipped with a unique Quadrupole Ion Trap Time of Flight MS (QitTof MS), which provides extremely fast resolution and sorting of ions of analytes. There have been only limited publications on the use of a QitTof MS, as Syagen has only recently perfected the device [48,51]. Syage et al. published on the integration of a GC to the Syagen QitTofMS for CWA detection [52] but Eckenrode and Whitchurch were the first to adapt a GC injector into a fast GC column for sample introduction by SPME into the FieldMate™. Their preliminary work with Syagen, Inc. is still unpublished other than via a lecture [51] and concentrated on the use of a dual electron impact/photoionization source, miniaturization of the device, and possible field use.

This research was based on connecting a fast-GC inlet to a prototype LPPI-MS detection system, thus providing the ability to concentrate and introduce a sample by SPME for analysis with a relatively fast resolution capability (the flash-GC) and very specific identification of CWA precursors and common interferents (the LPPI-MS). Similar systems have been proposed by Syagen but are not currently in production (the

Eckenrode/FBI Academy system previously mentioned is a prototype) [51,53]. The research presented in this manuscript is different in that SPME was the only sampling method evaluated, by headspace vice direct sampling, using a longer GC column, and with several new chemicals in addition to those used in research by Eckenrode et al. [51].

## **IV. Literature review**

### **IV A. Hydrogen cyanide**

#### *1.1 HCN Literature review*

Detection methods which are sensitive and amenable to field use are highly desirable for testing remote municipal water facilities as well as water supplies for deployed military troops. Current detection methods for aqueous cyanide contamination include spectrophotometric distillation, titration, and test strips based on a chemical reaction color change [54]. The various limits of detection of these methods are listed in Appendix 7.

Current GC-MS research on identifying and quantifying cyanide is mainly based on biological indices such as HCN in blood from fire exposure and poisoning [25,55]. Use of SPME or GC-MS for analysis of cyanide has been limited. Smith et al. optimized a method for 2 min passive SPME sampling for HCN in air with an 85  $\mu\text{m}$  CAR/PDMS SPME fiber for analysis with a GC-Nitrogen Phosphorus Detector using a GS-GasPro column [56].

Field detection of cyanide at approximately 8 ppm (8 mg/L) was chosen as an appropriate starting point for the working range for this research based on the Department of Defense (DOD) Short Term standard for drinking water (6 ppm, 6 mg/L) [54]. Most

common aqueous cyanide detection methods are not able to identify a wide range of organic compounds. A GC-MS detection system provides the advantage of potential confirmatory identification and quantitation of free cyanides in water as well as identification of other chemical pollutants.

## **IV B. Diisopropylamine**

### *1.1 DIPA literature review*

No previous studies that utilized GC-MS for the specific identification of DIPA were found. Generic CWA GC-MS methods should be suitable for identifying DIPA, based on the chemical similarity between DIPA and nerve agents. For air sampling, DIPA can be collected in 0.1 N sulfuric acid impingers for analysis by GC- flame ionization detector, with a detection range of 8.5 - 37.4 mg/m<sup>3</sup>. DIPA in food can be detected by GC-flame photometric detection after derivitization with benzene sulfonyl chloride. HPLC has also been used for DIPA detection [6]. DIPA has been successfully detected as a VX degradant and precursor by liquid chromatography-electrospray ionization-mass spectrometry (no detection limits given) [10] and as a hydrochloric acid-derivitized salt by high pressure liquid chromatography (HPLC) with an ultraviolet (UVC) detector with a range from 71-300 pg [57].

#### **IV C. Dimethyl methylphosphonate**

GC-GC-Time of Flight MS [58] and LC-MS [59] have been used for DMMP detection. Similar compounds are routinely detected by GC-MS [10] and microcolumn liquid chromatography and capillary electrophoresis with flame photometric detection [60].

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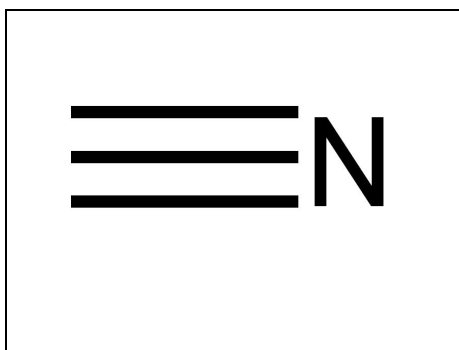
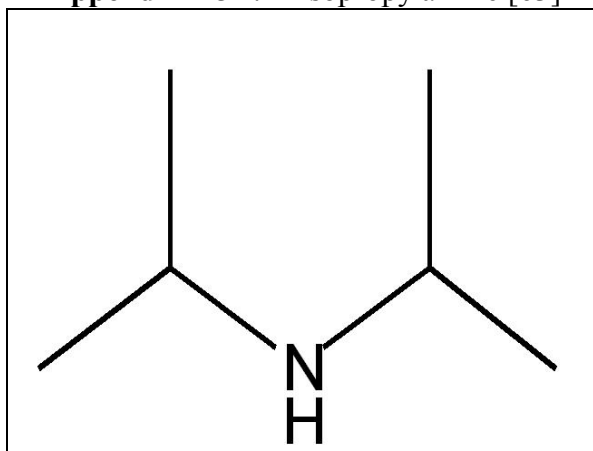
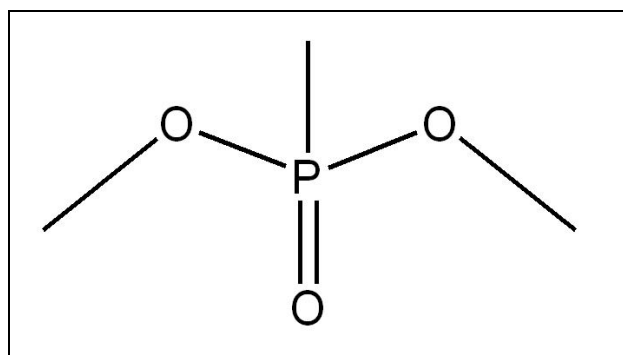
## APPENDICES

### Appendix 2-1. Acronyms and Abbreviations

APPI	Atmospheric pressure photoionization
BTEX	benzene, toluene, ethylbenzene, xylenes
CAR/PDMS	carboxen/polydimethylsiloxane
CBIRF	Chemical Biological Incident Response Force
CE	capillary electrophoresis
CWA	chemical warfare agent
CW/DVB	carbowax/divinylbenzene
DI	deionized
DIPA	diisopropylamine
DMMP	dimethyl methylphosphonate
DOD	Department of Defense
DRDC	Defence Research Development, Canada
eV	electron-volt
FTIR	Fourier Transform Infrared spectrometry
GC	gas chromatography
HCN	hydrogen cyanide
HPLC	high pressure liquid chromatography
IDLH	immediately dangerous to life and health
IMS	ion mobility spectrometry
LC	liquid chromatography
LPPI	low pressure photoionization
min	minutes
mL	milliliter
MS	mass spectrometry
<i>m/z</i>	mass-to-charge ratio
OPCW	Organisation for the Prohibition of Chemical Weapons
OSHA	Occupational Safety and Health Agency
PA	polyacrylate
PDMS	polydimethylsiloxane
PDMS/AC	polydimethylsiloxane with 10% activated charcoal
PDMS/DVB	polydimethylsiloxane/divinylbenzene
PEL	permissible exposure limit
PI	photoionization
QitTofMS	Quadrupole Ion Trap Time of Flight Mass Spectrometer
<i>s/n</i>	signal-to-noise ratio
SAW	surface acoustic wave
SPDE	solid phase dynamic extraction
SPME	solid phase microextraction
STEL	short term exposure limit
TIC	toxic industrial chemical
μL	microliter
USMC	United States Marine Corps

### Appendix 2-2. Physical and Chemical Characteristics

Parameter	Hydrogen Cyanide [5,61]	Diisopropylamine [6, 61]	Dimethyl methylphosphonate [61]
Molecular Formula	H-C-N	((CH <sub>3</sub> ) <sub>2</sub> CH <sub>2</sub> )NH	C <sub>3</sub> H <sub>9</sub> O <sub>3</sub> P
CAS	74-90-8	108-18-9	756-79-6
PK	pKa 9.2	pKa: 11.07 (in water) at 25 °C. pKb = 3.43 at 20 °C	N.D.
Molecular Weight	27.03	101.2	124.08
Melting Point (°C)	-13	-61	N.D.
Boiling Point (°C)	26	84	181
Vapor Pressure (mm Hg @25 °C)	742	79	0.962
Vapor Density g/L (Air=1)	0.94	3.5	4.2
K <sub>OW</sub>	0.56	25.1	0.25
K <sub>OC</sub>	0	140 (derived from experimental log K <sub>ow</sub> )	N.D.
Water Solubility (mg/L @ 25 °C)	Miscible, 1 × 10 <sup>6</sup>	Miscible, 1.1×10 <sup>5</sup>	Miscible, 1.1×10 <sup>6</sup>
Atmospheric OH Rate constant (cm <sup>3</sup> /molecule-sec)	3 × 10 <sup>-14</sup> exper.	9.98×10 <sup>-11</sup> estim.	5.71×10 <sup>-12</sup> estim.
Henry's Law Constant (atmxm <sup>3</sup> /mole)	1.33 × 10 <sup>-4</sup>	9.65×10 <sup>-5</sup> estim.	1.25×10 <sup>-6</sup> estim.
Density/Specific Gravity (g/ml @ 20 °C)	0.687	0.7169	1.150
Primary ions by EI [62]	27 (molecular), 26	44, 86, 58, 101 (molecular)	94, 79, 124 (molecular)
Odor	Bitter, almond-like	Ammonia or fish-like odor. Odor threshold = 1.8 ppm	N.D.
Initial State at STP	Liquid	Colorless liquid	Colorless liquid
PEL	No PEL. IDLH 50 ppm STEL 4.7 ppm/5 mg/m <sup>3</sup> , skin designation	5 ppm/20 mg/m <sup>3</sup> , skin designation. IDLH 200 ppm.	None.
Solubility notes	Miscible	Very soluble in acetone, benzene, ether, and ethanol.	Soluble in water, alcohol, ether.
Flash Point (open cup, °C)	-18	-7	43
Notes	1 ppm = 1.12 mg/m <sup>3</sup>	May attack some forms of plastic. 1 ppm = 4.21 mg/m <sup>3</sup>	1 ppm = 5.07 mg/m <sup>3</sup>

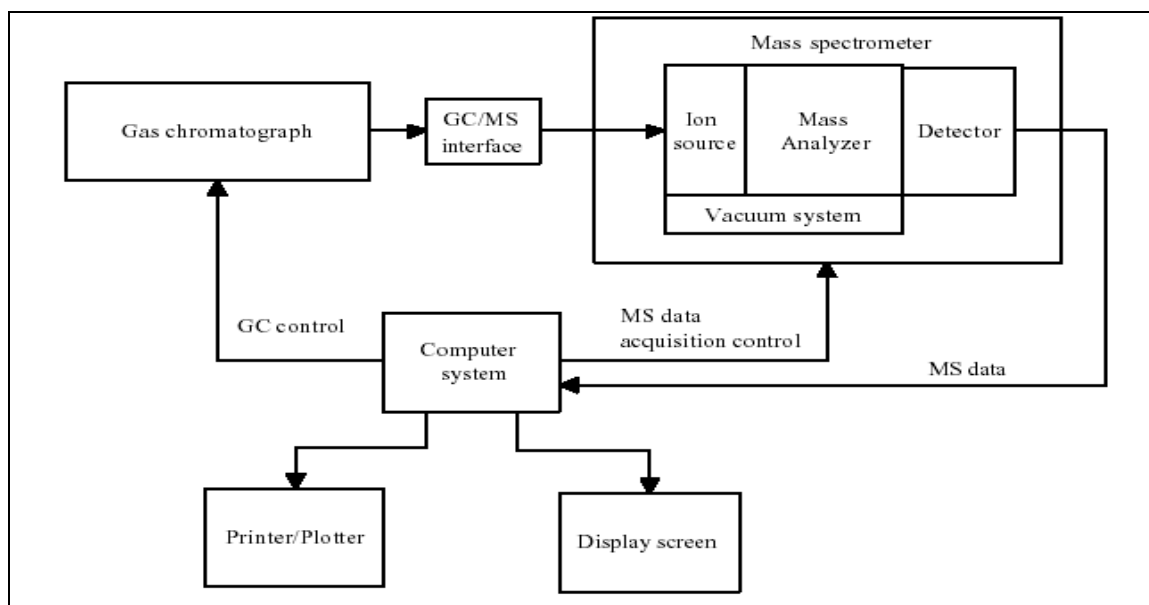
**APPENDIX 2-3. Molecular Structures of Selected Precursors****Appendix 2.3A. HCN [63]****Appendix 2-3B. Diisopropylamine [63]****Appendix 2-3C. Dimethyl methylphosphonate [63]****Appendix 2-4. Toxic Properties of Selected Precursors**

<b>Chemical</b>	<b>Toxic doses</b>
Cyanide salts	The oral LD <sub>50</sub> for NaCN and KCN is 1 and 2 mg/kg for a human adult, respectively [5].
DIPA	The LD50 in rats was 770 mg/kg orally and 4,800 mg/m <sup>3</sup> /2 hrs by inhalation [6].
DMMP	In rats, the oral LD <sub>50</sub> is 1050 mg/kg (IV) and 8,210 mg/kg (oral) [7,64].



**Appendix 2-5.** Comparison of HCN and Chemical Warfare Agents [5,24,54,65]

<b>Chemical Agent or Class</b>	<b>Human LC<sub>50</sub> (mg-min/m<sup>3</sup>) (air delivery)</b>	<b>LD<sub>50</sub> (mg/kg body wt) (Other routes; human unless noted)</b>
HCN	2,500-5,000 (unconsciousness in 30 seconds, death in 5-8 minutes). 45-54 may be tolerated for 0.5-1.0 hr	Intravenous 1. Liquid on skin 100. 50 mg oral dose in adult.
Cyanogen chloride	3,000	6 mg/kg (cat). > 1 g KCN ingested tolerated in humans.
Nerve agents	10-200	0.1 to 350 for liquid on skin; ingestion N.D.
Blister agents	900-5000	500-2000 by skin, ingestion N.D.

**Appendix 2-6. GC-MS Block Diagram [66]**

**Appendix 2-7. Limits of Detection for Specific Cyanide Methods [26,54,67-69]**

<b>Chemical</b>	<b>Method</b>	<b>Limit of Detection (ppm)</b>
Total cyanides or HCN as free cyanides	Hand-held spectrophotometric distillation methods (EPA Method 335.2)	0.02
Total cyanides	Automated spectrophotometric distillation methods (EPA Method 335.3)	0.005
Total cyanides	Selective electrode distillation (EPA Standard Method 4500)	0.05
HCN as free cyanides	M272 Chemical Agent Detection Kit	20
HCN as free cyanides	U.S. Army Interim Field Water Test Kit	1
HCN as free cyanides	EM Science colorimetric test strips	1
HCN as free cyanides	HachDREL 2010	0.001
HCN as free cyanides	Flow Injection, Ligand Exchange, and Amperometry (EPA Method OIA-1677)	0.0005

## CHAPTER 3

### DETECTION OF CYANIDE IN WATER BY SOLID PHASE MICROEXTRACTION AND GAS CHROMATOGRAPHY-MASS SPECTROMETRY ANALYSIS

Douglas K. Parrish, Philip A. Smith, Robert Fitz, Gary L. Hook

#### **Abstract**

Solid phase microextraction-gas chromatography-mass spectrometry was used to detect aqueous KCN as HCN in the headspace above acidified samples. Sampling 0.3 to 33.4 ppm solutions of  $\text{CN}^-$  for 5.0 min at 30 °C gave a linear correlation for HCN peak area plotted against concentration. A >3 times signal to noise ratio was obtained for HCN peak areas at levels as low as 0.3 ppm  $\text{CN}^-$ , and as low as 0.07 ppm by selected ion monitoring. The method was successfully field tested in the presence of common organic contaminants in three water types and is applicable for detection of cyanide and other volatile chemicals in water.

*Keywords:* Cyanide, HCN, drinking water contaminants, SPME, GC-MS

#### **1.1. Introduction**

##### *1.1 Background*

There are many chemicals that can be present in drinking water as pollutants or intentional contaminants. Cyanide salts, such as KCN and NaCN, are one such class of

chemical. Untreated water supplies, production facilities, distribution systems and storage facilities are all potentially susceptible to cyanide contamination, which can pose a health risk to civilian and military populations.

Cyanide is used in numerous processes in industrial nations, including plating and other metallurgical processes such as silver and gold refining, and as an intermediate in the manufacture of resin monomers, methacrylates, and nitriles. With U.S. demand in 2002 at 725,000 metric tons, the potential for inadvertent release to the environment is present [1]. Cyanide poisoning is still widely used to stun fish in Third World salt- and fresh waters as a method of gathering the fish for eating, and for tropical aquarium suppliers [2]. Other than individual and small group poisonings by cyanide-laced beverages, public water supplies in the U.S. have not yet been purposefully attacked [3]. However, the potential for intentional and unintentional contamination cannot be discounted.

Sensitive and field friendly detection methods for aqueous cyanide are highly desirable for testing remote municipal water facilities as well as water supplies for deployed military troops. The 1996 U.S. tri-service (Department of Defense or DoD) short term maximum standard for drinking water based on 5 L of water consumption per day per person is 6 mg/L of free cyanide. Onsite water monitoring is normally performed using spectrophotometric, titration, or colorimetric test strip methods that are specific for a few key analytes such as cyanide and fluorides, while analyses for organic chemicals and metals are normally performed in a laboratory setting [4,5]. The U.S. military M272 Chemical Agent Detection Kit can identify the presence of cyanide down to 20 ppm (weight/volume) in water, well above the short-term exposure level of interest [5]. The

U.S. Army field water test kit can detect cyanide from 1.0 – 30.0 ppm, although more training is required for its use compared to the M272 kit [6]. For public water supplies, the United States Environmental Protection Agency (EPA) maximum concentration level for cyanide in drinking water is 0.2 ppm [7].

### *1.2 Health Effects*

Though not considered to be as toxic as some chemicals via air delivery, cyanide is fairly easily found, prepared, and disseminated, especially for water delivery [8]. KCN, CaCN, and NaCN are common cyanide salts that disassociate in water. Cyanide poisoning by ingestion, inhalation, or dermal exposure can be quite rapid through interference with cell respiration processes. The oral LD<sub>50</sub> for NaCN and KCN is 1 and 2 mg/kg for an adult, respectively [9].

### *1.3 Field sampling/analysis*

Solid phase microextraction (SPME), when combined with gas chromatography-mass spectrometry (GC-MS) analysis, has been shown to be adaptable to sampling of various chemicals [10-14], including a chemical warfare agent in a field setting [15]. SPME use and theory have been well described [16,17].

Current GC-MS research targeting cyanide is mainly based on biological indices such as HCN in blood from fire exposure or poisoning [18]. Previously, SPME-GC-MS [19] and SPME-GC with nitrogen phosphorus detection [20] have been used for sampling cyanide in blood. Analysis by GC-MS for cyanide in water has been limited. Smith et al. [21] used passive 2.0 min SPME sampling to detect HCN as an air contaminant in field

samples. In that work, analysis was completed in a laboratory, and a porous layer open tubular (PLOT) column GC with a nitrogen-phosphorus detector was primarily used. A GC-MS detection method would provide the advantages of potential confirmatory identification and quantitation of free cyanides in water, as well as identification of other chemical pollutants, even unexpected analytes, so long as the selectivity of the SPME fiber coating and GC column stationary phase allowed analysis.

In this work, methods were explored for the detection of cyanide in treated and untreated fresh water samples using SPME and GC-MS. Field detection of cyanide near the DOD Short Term drinking water standard of 6 ppm was chosen as an appropriate starting point for this research. Successful development of methodology based on this approach could prove useful for protection of water supplies generated and maintained by deployed military personnel, and for civilian municipalities.

## **2. Materials and methods**

### *2.1 Materials*

Reagent grade KCN was purchased from Fisher Scientific (Fairhaven, NJ, USA). Sodium sulfate (Acros Organics, Morris Plains, NJ, USA) and sulfuric acid (LabChem, Inc, Pittsburgh, PA, USA) were used to drive the  $\text{CN}^-$  out of the water by saturation and acidification. Sample vials were 20 mL clear glass with 20 mm silicone-polytetrafluoroethane (PTFE) septum caps (MicroLiter Analytical Supplies, Suwanee, GA, USA). The deionized water used for the  $\text{CN}^-$  stock solution and for serial dilutions came from an installed Millipore® MilliQ deionized reverse osmosis water purification system (Milford, MA, USA). Tap water and pond water were locally obtained (Bethesda,

MD, USA). Standards for methyl tert-butyl ether (MTBE) and benzene, toluene, ethylbenzene, and xylenes (BTEX) were obtained from Aldrich (Milwaukee, WI, USA).

## 2.2 GC-MS methods

Analysis to detect aqueous  $\text{CN}^-$  as HCN in the headspace above an acidified sample was initially performed on a benchtop 6890 series gas chromatograph with a 5973 quadrupole mass selective detector (Agilent Technologies, Wilmington, DE, USA). All initial trials (optimal sampling temperature, time, acidification, and introduction of hydrocarbon contaminants) were performed on the laboratory instrument. The GC was fitted with a GS-GasPro PLOT, 30 m  $\times$  0.32 mm I.D. column (J&W Scientific, Folsom, CA, USA). Helium at 2.0 mL/min (constant flow mode) was used as the carrier gas. A 0.75 mm I.D. deactivated injection port liner (Supelco, Bellafonte, PA, USA) was used to provide rapid transfer of desorbed analytes onto the front of the column. The oven was programmed to hold at 60 °C for one min, ramp at 25 °C per min to 175 °C, then ramp at 35 °C per min and hold at 260 °C for 5.0 min. Desorption of the SPME fiber samples was accomplished in the splitless injection mode for 2.0 min, followed by 50 mL/min injector purge. The injector temperature and MS transfer line temperatures were held constant at 250 °C and 280 °C, respectively. Electron impact ionization (70 eV) was used and mass spectra were collected over the range of 10-250 mass to charge ( $m/z$ ). Selected ion monitoring (SIM) was employed for detection of cyanide at 0.5 and 0.07 ppm using the 26 and 27  $m/z$  ions. Sample retention characteristics and mass spectra were stored using the Agilent Chemstation software package.



An Agilent 6890 GC with a 5973 mass spectrometer was used for field analyses. This instrument was mounted in a van as a mobile laboratory and was similarly outfitted as the laboratory GC-MS but without an autosampler. A 10 m section of 0.18 mm I.D. deactivated transfer line was installed ahead of the 30 m GS-GasPro column as the van-mounted MS system was equipped with a diffusion pump while the benchtop model utilized a high performance turbo pump. High purity H<sub>2</sub> carrier gas from water electrolysis was provided at a constant head pressure of 15 psi for analyses completed in the field with this instrumentation system.

### *2.3 Solid Phase Microextraction (SPME)*

The choice of the 85 µm Carboxen/Polydimethylsiloxane (CAR/PDMS) SPME fiber for this research was based on previous work by Smith et al. [21]. The 85 µm Carboxen/PDMS Stableflex™ SPME fibers and holders are commercially available and were obtained from Supelco (Bellefonte, PA). Manufacturer's specifications for pre-use conditioning were followed.

For laboratory analyses, automated headspace sampling was carried out using a CTC CombiPAL LEAP GC sampler (LEAP Technologies, Inc., Carrboro, NC, USA), equipped with a combination digital heater/stirrer. The CombiPAL individually heated and stirred (700 RPM constant) each sample for 10.0 min prior and then sampled the vial headspace using SPME for the appropriate time. Upon completion of sampling, the SPME fiber was immediately placed in the injection port by the autosampler where the analytes were thermally desorbed. For field work, a manual fiber holder was used to

introduce the fiber into the vial via the silicone-PTFE septum and then into the mobile GC-MS injection port immediately after sampling.

#### *2.4 Sample preparation*

A stock solution was prepared by mixing KCN with deionized water (66.8 ppm  $\text{CN}^-$ , w/v, volumetric dilution). Sample preparation was accomplished as follows: a 1 mL sample of the  $\text{CN}^-$  stock solution was injected into a 20 mL lipped clear glass vial suitable for capping. Serial dilutions were then made with deionized water for a 2 mL volume in each vial. Salting with  $\text{Na}_2\text{SO}_4$  and acidification with  $\text{H}_2\text{SO}_4$  were used for all samples (except some of those created to study the effects of acidification and salting) to drive the cyanide out of solution and into the headspace as HCN. Samples were prepared without acidification, and caps were temporarily placed on the vials while awaiting salting. Sodium sulfate (1.0 g) and an 8 mm x 3 mm stir bar (Fisher Scientific, Fairhaven, NJ) were placed into the 20 mL vial. The silicone-PTFE septum cap was then permanently crimped onto the vial. The vial was placed on an ambient temperature ( $\sim 22^\circ\text{C}$ ) magnetic stir plate and agitated at a constant rate of 700 RPM for 5 min. Sulfuric acid (0.25 mL) was injected through the septum into the vial with a syringe just prior to sampling, thus forming the standard solution (2.0 mL stock solution + 1.0 g  $\text{Na}_2\text{SO}_4$  + 0.25 mL  $\text{H}_2\text{SO}_4$ ). For several samples, mixtures were made with local pond or tap water in place of the deionized water. The pond and tap water samples were prepared approximately 15 min after the water was drawn from the supply (faucet or pond). The pond water used was visibly cloudy, apparently from the presence of suspended organic matter.

## *2.5 Method optimization*

### *2.5.1 Selection of optimal sampling temperature*

Using the laboratory-based GC-MS instrument, sampling was performed at 5 temperatures (10 °C increments) ranging from 30 to 70 °C for 8.4 ppm CN<sup>-</sup> samples (acidified and with salt added).

### *2.5.2 Selection of optimal sampling time*

Using the previously optimized sampling temperature and the laboratory-based instrument, an uptake curve was developed by analysis of 8.4 ppm CN<sup>-</sup> samples (acidified and with salt added). Triplicate samples were collected for 0.5, 1, 5, 15, 30, 45, and 60 min. Sampling was then performed for 1, 5, and 15 min at various concentrations (1.1, 2.1, 4.2, 16.7, and 33.4 ppm of CN<sup>-</sup>) to check the linearity of the method for peak area plotted against concentration with different sampling times.

### *2.5.3 Effects of the addition of salt and acid to samples*

Using the laboratory-based GC-MS instrument, the resulting extracted 27 *m/z* ion peak areas were compared for samples created using an 8.4 ppm CN<sup>-</sup> solution with both acidification and salting, with acidification only, with addition of salt only, and with neither acid nor salt added.

## *2.6 Method sensitivity*

Sensitivity was determined using the optimized sampling temperature, acidification, and salting with the laboratory GC-MS system. Measurements were made

from serial dilutions of  $\text{CN}^-$  (0.3 to 33.4 ppm) with 5.0 minute sampling for full range scans (10-250  $m/z$ ) and at 0.07 and 0.5 ppm with 5.0 min sampling for SIM scans (26 and 27  $m/z$  ions).

### *2.7 Analysis of cyanide in deionized, tap, and pond water, and in hydrocarbon-contaminated samples*

Comparisons of the benchtop and mobile GC-MS systems were made for pond, tap, and deionized water with  $\text{CN}^-$  at 8.4 ppm and 1.1 ppm to verify that both systems could be used to detect  $\text{CN}^-$  in a limited variety of water types. Secondly, other possible low level water contaminants (10 ppm BTEX and MTBE) were used to challenge the method on both GC-MS systems by spiking these contaminants during initial preparation of 8.4 ppm  $\text{CN}^-$  pond, tap, and deionized water samples.

### *2.8 Statistical analysis*

Experimental data were examined for differences between extracted 27  $m/z$  ion peak areas. To examine reproducibility, the samples were run in triplicate and relative standard deviation (RSD) values were calculated. A One-Way Analysis of Variance (ANOVA) test was completed for each of the extraction time, temperature, water type, and sample preparation comparisons. This was followed by Tukey's post hoc comparison to examine the source of variability.

### 3. Results and discussion

#### 3.1 Sampling temperature selection

Table 3-1 displays the data resulting from the extraction temperature optimization experiments. Extractions performed at 30 °C and 40 °C provided the best sensitivity as demonstrated by the extracted 27 *m/z* ion peak area. At a significance level of 0.05, the peak areas obtained at 30 °C were not significantly different than peak areas obtained at 40 °C. However, 30 °C was significantly different than 50 °C and was therefore employed in all subsequent experiments.

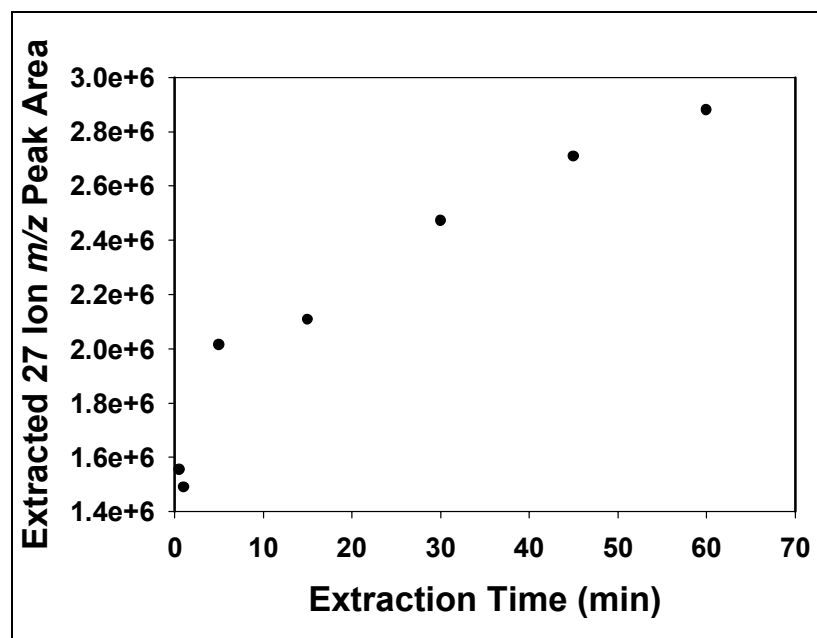
**Table 3-1.** Optimal temperature selection, benchtop GC-MS 27 *m/z* HCN peak area counts for 8.4 ppm CN<sup>-</sup> samples, 5.0 min extraction time, CAR/PDMS SPME fiber.

Sample #	Sampling temperature				
	30 °C	40 °C	50 °C	60 °C	70 °C
<b>1</b>	2.19-10 <sup>6</sup>	1.77-10 <sup>6</sup>	1.42-10 <sup>6</sup>	9.99-10 <sup>5</sup>	8.33-10 <sup>5</sup>
<b>2</b>	1.87-10 <sup>6</sup>	1.58-10 <sup>6</sup>	1.34-10 <sup>6</sup>	8.42-10 <sup>5</sup>	8.01-10 <sup>5</sup>
<b>3</b>	1.99-10 <sup>6</sup>	1.52-10 <sup>6</sup>	1.29-10 <sup>6</sup>	8.81-10 <sup>5</sup>	7.49-10 <sup>5</sup>
<b>Mean</b>	2.01-10 <sup>6</sup>	1.62-10 <sup>6</sup>	1.37-10 <sup>6</sup>	9.07-10 <sup>5</sup>	7.94-10 <sup>5</sup>
<b><sup>1</sup>SD</b>	1.63-10 <sup>5</sup>	1.30-10 <sup>5</sup>	8.76-10 <sup>5</sup>	8.20-10 <sup>4</sup>	4.24-10 <sup>4</sup>
<b><sup>2</sup>RSD</b>	0.08	0.08	0.06	0.09	0.05
<b>Notes:</b>					
1= Standard Deviation					
2= Relative Standard Deviation					

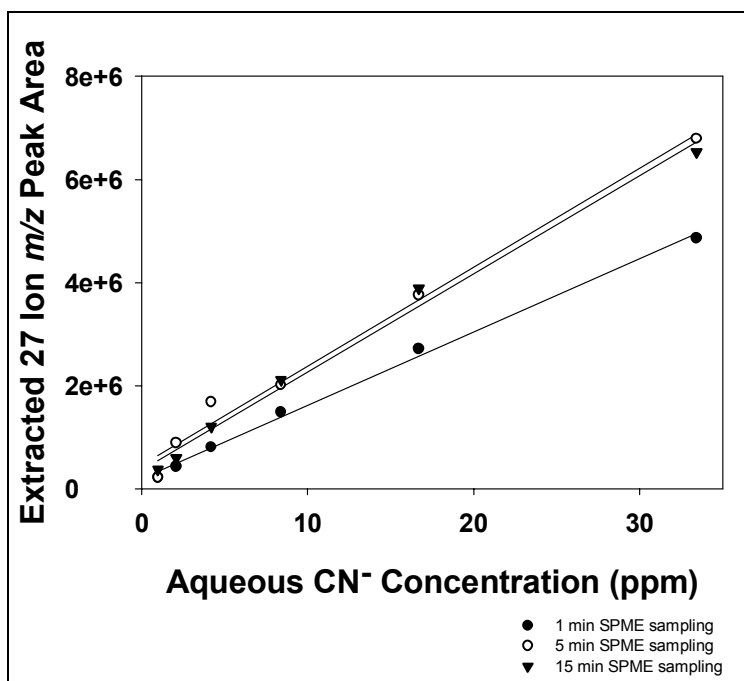
#### 3.2 Sampling time selection

Figure 3-1 is the HCN uptake curve showing the optimal extraction time was 45.0 min with 30 °C extraction temperature. Extraction for 45.0 min was not significantly different from 30.0 and 60.0 min; however, 30.0 min samples were significantly different

than 60.0 min sampling peak area responses (extracted 27  $m/z$  ion HCN peak areas). Even though equilibrium was apparently approached around 45.0 min, 5.0 min was chosen as the sampling time as it is better for field analysis due to the faster sample throughput while maintaining comparable sensitivity. Sampling for 5.0 min provided 74.4% of the peak area response of sampling for 45.0 min. A 5.0 min extraction at 30 °C of concentrations ranging from 0.3 – 33.4 ppm showed good linearity ( $R^2 = 0.983$ ). For these samples, when repeating completion of triplicate samples it was noted that below 1.1 ppm the RSD values were  $>0.10$ . Figure 3-2 provides a graphic display comparing 27  $m/z$  peak areas for HCN with 1.0, 5.0, and 15.0 min extraction times. The 5.0 min results were similar to those obtained with 15.0 min sampling.



**Figure 3-1.** Headspace SPME uptake curve, full scan GC-MS extracted 27  $m/z$  ion current average peak area for aqueous  $CN^-$  at 8.4 ppm plotted against SPME sampling time, with salt and acid added (CAR/PDMS, 30 °C).



**Figure 3-2.** Average of GC-MS extracted 27  $m/z$  ion current peak areas at each concentration (0.3 to 33.4 ppm aqueous  $\text{CN}^-$ ), 1, 5, and 15 min extractions, with salt and acid added (CAR/PDMS, 30 °C).

### 3.3 Effects of addition of salt and acid to samples

The results of sampling with varied acidification and salt use are given in Table 3-2. Tested at 8.4 ppm of  $\text{CN}^-$ , the 27  $m/z$  peak was readily apparent even without adding salt, acid, or neither salt nor acid to the sampling mixture. However, withholding any of these ingredients decreased the resulting peak areas. The addition of acid and salt (the “standard” mixture) gave the best response. The resulting 27  $m/z$  HCN peak areas were significantly different ( $p = 0.04$ ) from the other mixtures. Leaving the salt out but adding acid decreased the peak areas, and leaving the acid out but adding salt decreased the peak area even more. The samples with neither salt nor acid added gave the poorest response overall.

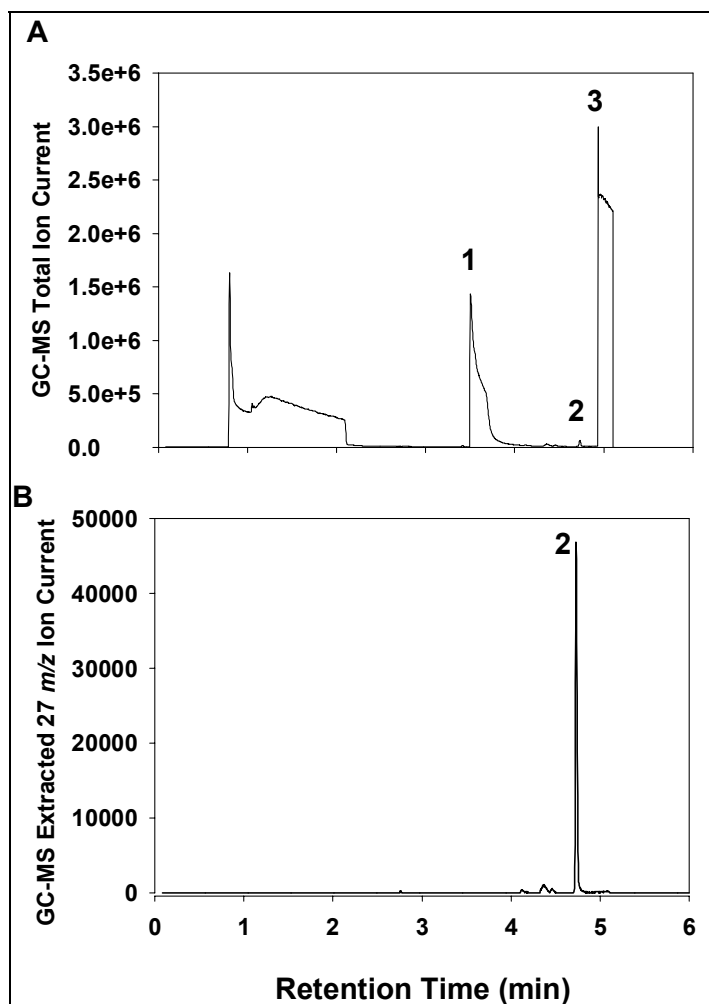
**Table 3-2.** Comparison of addition of salt/acid effect for 27 *m/z* HCN peak area counts for 8.4 ppm CN<sup>-</sup> samples (5.0 min extraction time, 30 °C, CAR/PDMS SPME fiber).

<b>Salting/Acidification Strategies</b>				
	<b>No acid or salt</b>	<b>Acid only</b>	<b>Salt only</b>	<b>Salt + acid</b>
<b>Sample #</b>				
<b>1</b>	1.01-10 <sup>6</sup>	1.05-10 <sup>6</sup>	1.47-10 <sup>6</sup>	2.19-10 <sup>6</sup>
<b>2</b>	9.76-10 <sup>5</sup>	1.24-10 <sup>6</sup>	1.43-10 <sup>6</sup>	1.87-10 <sup>6</sup>
<b>3</b>	1.02-10 <sup>6</sup>	1.05-10 <sup>6</sup>	1.66-10 <sup>6</sup>	1.99-10 <sup>6</sup>
<b>Mean</b>	1.00-10 <sup>6</sup>	1.11-10 <sup>6</sup>	1.52-10 <sup>6</sup>	2.01-10 <sup>6</sup>
<b><sup>1</sup>SD</b>	2.30-10 <sup>4</sup>	1.08-10 <sup>5</sup>	1.25-10 <sup>5</sup>	1.63-10 <sup>5</sup>
<b><sup>2</sup>RSD</b>	2.30	9.76	8.21	8.08
<b>Notes:</b>				
1= Standard Deviation				
2= Relative Standard Deviation				

### 3.4 Method sensitivity

Based on a 5.0 min extraction at 30 °C (full scan range), we were able to quantify CN<sup>-</sup> down to 1.1 ppm and identify CN<sup>-</sup> down to 0.3 ppm. Figures 3-3A and 3-3B are representative total ion and extracted ion chromatograms of 1.1 ppm CN<sup>-</sup>. Identification of the extracted 27 *m/z* ion with 5.0 min sampling was possible at levels lower than 1.1 ppm, but quantitation was not reliable due to the variability in extracted ion peak areas and the very small size of the unextracted peak in a total ion current GC-MS chromatogram. Obtaining reproducible results when sampling for 1.0 min or less was difficult due to the steepness of this part of the uptake curve. However, 5.0 min extractions at 30 °C provided adequate sensitivity and reproducibility at a 1.1 ppm cyanide concentration in water, which is below the DoD short term maximum contamination level of 6 ppm. When employing SIM scan, 5.0 minute sampling provided identification with > 3:1 signal to noise ratio down to 0.07 ppm of CN<sup>-</sup>, but reliable quantification was not achievable at this concentration.





**Figure 3-3A.** SPME/GC-MS total ion chromatogram from analysis of 1.1 ppm aqueous  $\text{CN}^-$ , headspace SPME sampling, 5.0 min extraction, with salt and acid added (CAR/PDMS, 30 °C).

**Figure 3-3B.** SPME/GC-MS extracted 27  $m/z$  ion chromatogram from analysis of 1.1 ppm aqueous  $\text{CN}^-$ , headspace SPME sampling, 5.0 min extraction, with salt and acid added (CAR/PDMS, 30 °C).

Compound key for Figs. 3-3A and B: **1** sulfur dioxide<sup>1</sup>, **2** HCN<sup>2</sup>, **3** water<sup>1</sup>.

<sup>1</sup>Identification based upon EI spectrum match.

<sup>2</sup>Identification based upon EI spectrum match with authentic standard.

**NOTE :** MS turned off at 5.3 min.

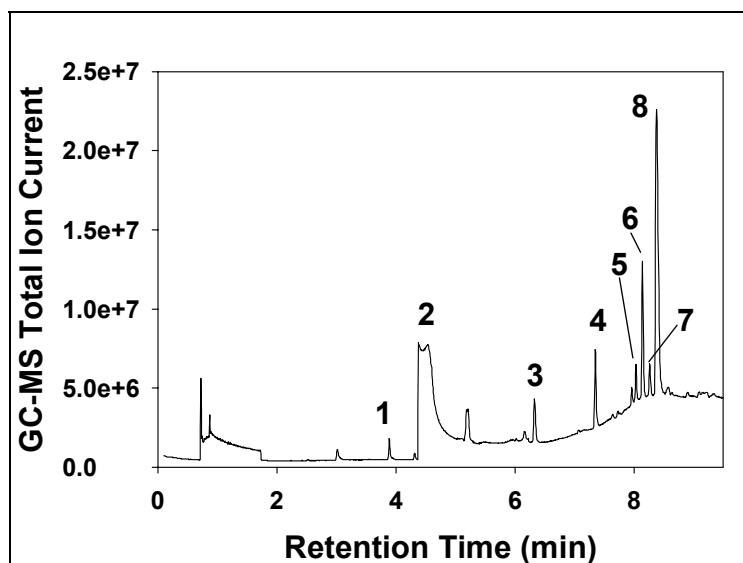
With a 30 min extraction at 30 °C, it was possible to achieve quantitation of  $\text{CN}^-$  at 0.3 ppm with an RSD of less than 0.08 and increased peak areas compared to 5 min

sampling. At 0.3 ppm, the signal to noise ratio on a total ion chromatogram for a 30 min sample was still greater than, but approaching 3:1.

### *3.5 Analysis of cyanide in deionized, tap, and pond water, and in hydrocarbon-contaminated samples*

Cyanide was successfully detected in deionized, pond, and tap water at 1.1 and 8.4 ppm  $\text{CN}^-$  concentrations using both the laboratory-based and van-mounted GC-MS instruments. Comparison of tap, pond, and deionized water samples spiked with the cyanide stock solution showed similar results at the 1.1 and 8.4 ppm level of  $\text{CN}^-$ . The extracted 27  $m/z$  ion peak areas for tap and deionized water were not significantly different from each other but the deionized water sample peak areas were significantly higher in response than the pond sample ( $p=0.04$ ).

Cyanide was successfully detected in the presence of common water contaminants, BTEX and MTBE. Tested at 10 ppm for BTEX and MTBE, spiked into both 1.1 and 8.4 ppm  $\text{CN}^-$  solutions, the contaminants did not impede the detection and quantification of cyanide in pond, tap, and DI water using either GC-MS system. Figure 3-4 shows a representative chromatogram obtained using the van-mounted GC-MS system under field conditions. The hydrocarbon contaminants are clearly observed, and identifiable by mass spectrum match, demonstrating that for suitable analytes, identification of unknown analytes is possible concurrently with detection of aqueous  $\text{CN}^-$ .



**Figure 3-4.** GC-MS chromatogram for 8.4 ppm aqueous  $\text{CN}^-$ , with 10 ppm BTEX and MTBE in tap water with salt and acid added, manual headspace SPME sampling, analyzed using van-mounted GC-MS under field conditions, (CAR/PDMS, 30 °C, 5 min extraction).

Compound key: **1**  $\text{HCN}^2$ , **2** water<sup>1</sup>, **3** benzene<sup>2</sup>, **4** toluene<sup>2</sup>, **5** ethylbenzene<sup>2</sup>, **6** m-, p-xylenes<sup>2</sup>, **7** o-xylene<sup>2</sup>, **8** MTBE<sup>2</sup>.

<sup>1</sup>Identification based upon EI spectrum match.

<sup>2</sup>Identification based upon EI spectrum and retention time match with authentic standard.

#### 4. Conclusions

A SPME-GC-MS headspace sampling and analysis technique based on 5.0 min sampling at 30 °C proved effective for detecting cyanide in water from 0.07 to 33.4 ppm. The 85  $\mu\text{m}$  CAR/PDMS fiber and GS-GasPro PLOT column provided linear, reliable identification and quantification for cyanide (1.0 - 33.4 ppm) and identification of some common water hydrocarbon contaminants. With the need for field sampling in mind, the techniques used to optimize extraction conditions were limited to heating, and adjustments in sample pH and saturation by addition of salt and acid. This method for sample preparation, analyte extraction, and GC-MS setup is suitable for initial analysis of drinking water supplies to meet U.S. DoD short term exposure limits for mobile forces in

the field that are equipped with suitable GC-MS instrumentation. It is also applicable for initial sampling by municipalities desiring a field screening method for a variety of chemical contaminants. However, sampling time would likely need to be increased and SIM-scanning used to reliably quantitate  $CN^-$  near the EPA-required maximum concentration level (0.2 ppm).

### **Acknowledgements**

We thank the U.S. Army Center for Environmental Health Research, through a contract with the Henry M. Jackson Foundation for the Advancement of Military Medicine, for providing funding to accomplish this research. CPL David Hoyle and CPL Aaron Rager, Mobile Laboratory Chemical Detection Technicians of the USMC Chemical Biological Incident Response Force were key participants in the field trials. Also, Dr. Thomas Johnson and LCDR Richard Erickson, Uniformed Services University, provided significant support during this research.

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## CHAPTER 4

### **FIELD EXPEDIENT DETECTION OF A CHEMICAL WARFARE AGENT PRECURSOR BY SOLID PHASE MICROEXTRACTION SAMPLING AND GAS CHROMATOGRAPHY-MASS SPECTROMETRY ANALYSIS**

Douglas K. Parrish, Philip A. Smith, Jerry Formisano, Steven Sorgen, Gary L. Hook

Keywords: DIPA, precursor, SPME, GC-MS

#### **Abstract**

Solid phase microextraction (SPME) methods for sampling diisopropylamine (DIPA), a precursor for the chemical warfare agent VX, in the headspace above soil and water matrices were developed in the laboratory and then evaluated in a field setting. Gas chromatography-mass spectrometry (GC-MS) analysis was used. Using relatively rapid extraction times, these methods gave a linear response for DIPA in soil (0.72 – 3584.5  $\mu\text{g}$  DIPA/g soil) and for DIPA in deionized water (0.018 - 17.9  $\mu\text{g/mL}$ ). The methods were successfully field tested with common hydrocarbon contaminants; diesel fuel in 3 common agricultural soil types, and benzene, toluene, ethylbenzene, and xylenes in 3 water types. Although SPME/GC-MS was successful at identifying unknowns, it was not reliable for quantification of DIPA in the presence of competing chemicals in complex matrices possibly due to competition for adsorption sites on the coating of the SPME fiber used.

## 1. Introduction

Emergency response and military field teams need specific methods for the detection of chemical warfare agents (CWAs), their precursors, and degradants. The same methods that are used for the detection and quantification of toxic industrial chemicals (TICs) may be applied by field teams so that potential CWA production sites can be differentiated from industrial chemical manufacturing facilities. These methods would also be applicable to assessing potential health risks associated with a terrorist release of chemicals and during incident recovery operations. To this end, military industrial hygienists and chemical detection experts need onsite detection methods that are sensitive and that can provide information about a compound's chemical identity and structure [1]. Ideally, methods used should also have the ability to discriminate between similar compounds. This is needed for positive identification of unknown chemicals in a complex mixture with background compounds and interferences resulting from a complicated substrate such as soil.

In this work, methods are explored for the field detection of diisopropylamine (DIPA) in the headspace above samples of 3 soil and 3 water types using solid phase microextraction (SPME) combined with gas chromatography-mass spectrometry (GC-MS) analysis. In an effort to develop a field-friendly sampling and analysis method, samples were only subjected to heating and stirring. Manipulation of the sample pH was not included in order to minimize the logistical burden associated with extended periods of fieldwork.



### *1.1 Background*

The goal of chemical detection teams is rapid field analysis of volatile and semi-volatile organic compounds. While an initial qualitative method is very useful, determination of chemical exposures as mandated by U.S. Presidential Review Directive 5 [2] is the end goal of field analyses to facilitate risk assessment and force health protection. The ability to reliably identify and then perform additional analyses to quantify chemicals in the environment during military deployment or domestic incident response is key to health surveillance [1].

GC-MS is a powerful 3-dimensional detection system well suited for definitive CWA analyses [3], but few field methods have been published. Laboratory identification methods for CWAs and their degradation products [4-9] are fairly well established but few methods are published for field or laboratory identification of CWA precursors.

SPME is useful for field sampling of CWAs [10] and other chemicals, especially when combined with GC-MS analysis [11-15]. SPME use and theory have been well established by Pawliszyn and others [16,17]. No published methods for DIPA sampling with SPME or identification by GC-MS are available. Organisation for the Prohibition of Chemical Weapons (OPCW) methods are generally intended for laboratory use and are not specifically designed to provide sample preparation and analysis methods suited for field detection. The OPCW has detailed methods for the detection of CWAs and selected precursors. The OPCW also maintains exhaustive lists of regulated chemicals [18-20].

DIPA is an intermediate precursor for production of the organophosphorus nerve agent *O*-ethyl *S*-(2-diisopropylaminoethyl) methylphosphonothiolate (VX). DIPA is also a potential by-product of hypochlorite decontamination of VX [4,21] and is used in the

synthesis of pesticides and pharmaceuticals [22]. DIPA poses a dual threat. It is useful as an intermediate precursor for CWA production as well as having harmful properties in its own right as an industrial chemical [20,22]. DIPA is a severe eye, respiratory, and skin irritant. In humans, exposure to high concentrations can lead to acute pulmonary edema and burns [22].

DIPA is expected to exist solely as a vapor in air with an estimated half-life of 4 hours. DIPA is not expected to readily volatilize from most moist soils (assuming neutral to mildly basic soil conditions), based on the high acid-base ionization constant of 11.7. DIPA is most likely to exist in soil in the protonated form based on the pKa, and thus will bind to organic content and colloidal clay in soils. In soil, DIPA is estimated to have a Koc of 140 and high mobility for the neutral species [22].

For air sampling, DIPA has been collected in 0.1N sulfuric acid impingers for analysis by GC-flame ionization detector, with a detection range of 8.5 to 37.4 mg/m<sup>3</sup> [22]. In food, DIPA has been analyzed by GC-flame photometric detector after derivitization with benzene sulfonyl chloride [23]. High performance liquid chromatography with an ultraviolet detector has also been used for DIPA detection [24].

## **2. Materials and methods**

### *2.1 Materials*

Reagent grade DIPA was purchased from Sigma Aldrich (Milwaukee, WI). Sample vials were 20 mL clear glass with 20 mm silicone-polytetrafluoroethane (PTFE) septum caps (MicroLiter Analytical Supplies, Suwanee, GA, USA). Three standard soil types were obtained from RT Corporation (Ogden, Utah, USA): Soil No. 1 (sandy loam),

Soil No. 2 (sandy clay loam), and Soil No. 3 (loam). Deionized (DI) water from a locally installed Millipore® MilliQ (Milford, MA, USA) deionized reverse osmosis water purification system was used. Diesel fuel, tap water, and stream water were locally obtained (Bethesda, MD, USA). Standards for benzene, toluene, ethylbenzene, and xylenes (BTEX), and 1,2,3 trimethylbenzene were obtained from Aldrich (Milwaukee, WI, USA).

## *2.2 Analytical methods*

All initial trials to detect DIPA in the headspace above water and soil samples were initially performed on a benchtop 6890 series gas chromatograph with a 5973 quadrupole mass selective detector (Agilent Technologies, Wilmington, DE, USA). Operating parameters are indicated in Table 4-1. Selected ion monitoring (SIM) was employed for low level detection of DIPA at 0.012 to 1.12 µg/mL in water and 0.18 to 3.6 µg DIPA/g soil with 5.0 min sampling using the 44 and 86 mass to charge ( $m/z$ ) ions. Full scan monitoring was employed for all other analyses. Sample retention characteristics and mass spectra were stored using the Agilent Chemstation software package. Automated headspace sampling was carried out with a CTC CombiPAL LEAP GC sampler (LEAP Technologies, Inc, Carrboro, NC, USA).

**Table 4-1.** GC-MS Operating Parameters

	<b>Benchtop, Agilent 6890/5973</b>	<b>Mobile, Agilent 6890/5973 + Flash GC</b>
Column	DB-1, 30 m × 0.25 mm I.D. × 1.0 µm column (J&W Scientific, Folsom, CA, USA).	DB-5, 30 m × 0.25 mm I.D. × 0.25 µm column (J&W Scientific).
Carrier gas	Splitless, 1.2 mL/min, helium	Splitless, 2.5 mL/min, hydrogen
Column ramping	45 °C for 2.0 min, 25 °C/min to 145 °C, 50 °C/min to 280 °C.	Oven = 200 °C. RVM column = 40 °C for 2.0 min, 60 °C/min to 100 °C, 10 °C/min to 110 °C, 200 °C/ min to 250 °C, hold for 73 sec.
GC Injector	270 °C	270 °C
MS transfer line	280 °C	280 °C
Electron impact ionization	70 eV	70 eV
Full scan mass range	10-250 <i>m/z</i> .	10-250 <i>m/z</i> .

The same type of GC-MS, mounted in a United States Marine Corps Chemical Biological Incident Response Force (USMC CBIRF) van as a mobile laboratory, with similar operating parameters (Table 4-1) was employed for field testing this method. A GC column was retrofitted as a flash GC, Low Thermal Mass A68 door unit (RVM Scientific Corp., Santa Barbara, CA, USA).

The following six fiber coatings were evaluated: 65 µm polydimethylsiloxane-divinylbenzene (PDMS-DVB), 7 µm and 100 µm PDMS, 85 µm polyacrylate (PA), 85 µm Carboxen- polydimethylsiloxane (CAR-PDMS), and 65 µm Carbowax-divinylbenzene (CW-DVB). The optimum SPME fiber was selected by headspace sampling for DIPA in a simple two-phase system. All fiber optimization extractions were performed at 30 °C for 15 sec in a vial containing 35.85 mg/m<sup>3</sup> DIPA.

### 2.2.1 Sampling procedure

All sampling was performed in the headspace of sealed 20 mL vials. For water sampling, stock and serial dilutions of DIPA were prepared in DI water, using a 10 mL sample size and an 8 mm  $\times$  3 mm stir bar (Fisher Scientific, Fairhaven, NJ). The vial was placed on an ambient temperature ( $\sim 22$  °C) magnetic stir plate (Corning, Acton, MA, USA) and agitated at a constant rate of 700 RPM for 5.0 min prior to being placed into the CombiPAL sampling block, where it was allowed to equilibrate at the sampling temperature for 5.0 min. Sandy clay loam soil samples (1.0 g) were spiked with neat DIPA or serial dilutions in methanol and hand agitated for 20 sec. The soil samples were then placed into the CombiPAL sampling block, where they were allowed to equilibrate at the sampling temperature for 5.0 min. Throughout, new samples were prepared for each measurement, and all measurements were made on 3 samples per series. In order to estimate the mass of DIPA loaded onto a SPME fiber, splitless injection analyses of liquid DIPA were made to obtain a curve with mass of analyte on-column plotted against extracted 44  $m/z$  ion peak area for 5 concentrations (0.7 to 716.9 ng).

Sampling by SPME was performed in both DI water and sandy clay loam soil substrates in 20 mL crimped topped vials. A 10 mL aliquot of 17.9  $\mu\text{g}$  DIPA/mL DI water was sampled for 5.0 min at 10 °C intervals from 30 to 70 °C. A 1 g soil sample containing 3584.5  $\mu\text{g}$  DIPA/g soil was also sampled for the same time period in the same temperature range. Using the optimized sampling temperature, uptake curves were developed by analysis of 17.9  $\mu\text{g}$  DIPA/mL DI water with extraction times of 1.0, 5.0, 15.0, 30.0, and 60.0 min. This was repeated with 3584.5  $\mu\text{g}$  DIPA/1.0 g soil using extractions times of 0.5, 1.0, 5.0, 15.0, and 30.0 min. Sandy clay loam soil and DI water

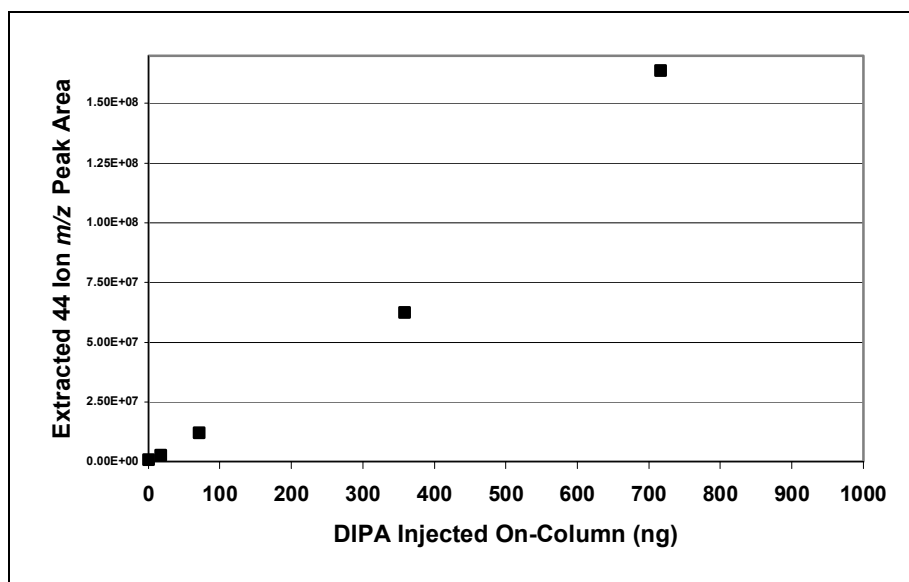
samples were then analyzed for method sensitivity and apparent limits of detection on the benchtop GC-MS.

The methods were then tested on both the benchtop and mobile GC-MS systems using 3 soil and water types contaminated with common hydrocarbon interferents. The 3 soils used were sandy clay loam, sandy loam, and loam. The 3 water types used were stream, tap, and DI waters. The soil samples analyzed in the Mobile Van were heated to ~40 °C to drive the vapors into the vial headspace due to the low ambient temperatures that day.

### **3. Results and discussion**

#### *3.1 Fiber selection and liquid injection calibration curve*

The PDMS/DVB fiber provided the optimum sensitivity by comparing the extracted ion peak areas from headspace sampling and was selected for the remainder of the study. The calibration curve for liquid injection analyses of DIPA with the benchtop GC-MS showed good linearity ( $R^2 = 0.9956$ ) (Figure 4-1). Estimation of the mass of DIPA loaded onto a SPME fiber is possible by correlating this liquid injection curve with the extracted 44 ion  $m/z$  peak areas obtained by SPME-GC-MS. PDMS/DVB fiber recovery efficiencies averaged 1% for DIPA in soil and water compared to liquid calibration injections.



**Figure 4-1.** GC-MS extracted 44 ion  $m/z$  peak area for direct injections of DIPA (0.7 – 716.9 ng) onto GC column.

### 3.2 Sampling temperature

Water sampling showed a linear relationship between the extraction temperatures. However, the results of sampling soil from 30 to 70 °C were curvi-linear (quadratic), possibly due to fugacity losses or matrix effects. Water sampling was optimal at 70 °C while soil sampling was optimal at 30 °C during 5.0 min sampling. Sampling 0.018 to 17.9 µg/mL solutions of DIPA in DI water for 5.0 min at 70 °C gave a linear correlation for DIPA peak area plotted against concentration. A >3 times signal to noise ratio was obtained for DIPA peak areas by selected ion monitoring at levels as low as 0.009 µg/mL in water.

Sampling soil at 30 °C for 5.0 min provided a significantly increased extracted 44 ion  $m/z$  peak area response compared to the other 4 temperatures. The p value was 0.036 by One Way ANOVA and Tukey's Post Hoc Analysis. The peak area responses in soil, while generally inversely related to temperature increase, were non-linear, possibly due

to matrix effects or fugacity losses. Sampling aqueous solutions of 17.9 µg/mL DIPA for 5.0 min at various temperatures gave a linear response ( $R^2$  value of 0.939 for the extracted 44 ion  $m/z$  peak areas). At a 5% significance level, the peak areas obtained at 70 °C were not significantly different than peak areas obtained at 60 °C for water samples. However, 70 °C was significantly different than 50 °C ( $p=0.003$ ). Variability in water samples was high when sampling at 30 and 40 °C and peak shapes were poorly formed. All subsequent water extractions were performed at 70 °C while soil was sampled at 30 °C.

### 3.3 Sampling time

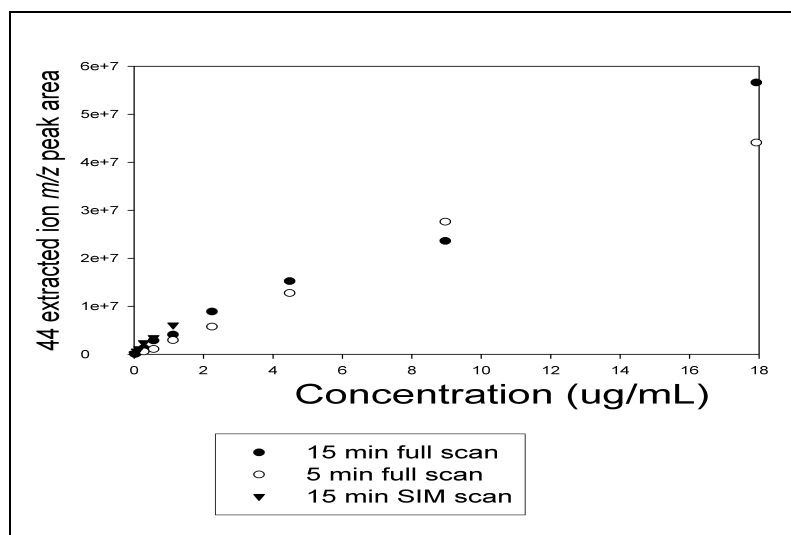
Equilibrium for headspace sampling of sandy clay soil samples was apparently reached by 5.0 min based on the 30 °C optimized extraction temperature. For soil sampling, the 5.0 min extraction was significantly different ( $p=0.014$ ) than both the 30 sec and 1.0 min extractions ( $p=0.046$ ). The 5.0 min extraction was not significantly different than 10.0, 15.0, or 30.0 min extractions ( $p=0.999$ , 0.874, and 0.710, respectively). For all further soil analyses, 5.0 min was used as the sampling time.

Equilibrium for headspace sampling of water samples was apparently reached by 5.0 min based on the 70 °C optimized extraction temperature at 17.9 µg/mL DIPA. Five min was significantly different than 1.0 min sampling when comparing extracted 44 ion  $m/z$  peak areas but not significantly different than 15.0, 30.0 or 60.0 min. But comparison of only 5.0 to 15.0 min sampling at 0.28 µg/mL DIPA showed that 15.0 min sampling provided significantly increased extracted 44 ion  $m/z$  peak area responses.



### 3.4.1 Method sensitivity in DI water

Employing the optimized sampling temperature, a comparison was made at various concentrations using 5.0 and 15.0 min sampling for DI water. Both the 5.0 and 15.0 min extractions at 70 °C showed good linearity over the concentration range sampled (0.28 to 17.9 µg/mL for 5.0 min sampling, 0.018 to 17.9 µg/mL for 15 min sampling). The  $R^2$  of extracted 44 ion  $m/z$  peak averages over the sampling range were 0.99975 and 0.9985, respectively. Next, SIM using the 44  $m/z$  ion was employed with 15.0 min extractions at 70 °C for concentrations ranging from 0.0088 to 1.12 µg DIPA/mL DI water. The graphic results of these 3 sampling strategies are shown in Figure 4-2. An extraction time of 5.0 min was used for all further studies as it provided the desired level of sensitivity and is more in line with the desire for a rapid, readily used field method. It is possible to achieve a significantly lower apparent limit of detection using a 15.0 min extraction time for both full scan and SIM scan analyses.



**Figure 4-2.** Comparison of GC-MS extracted 44  $m/z$  ion current average peak area response plotted against concentration for aqueous DIPA (0.0088 µg/ml to 17.9 µg/ml) for 5.0 min full scan, 15.0 min full scan, and 15.0 min SIM scans (PDMS-DVB, 70 °C).

### 3.4.2 Method sensitivity in soil

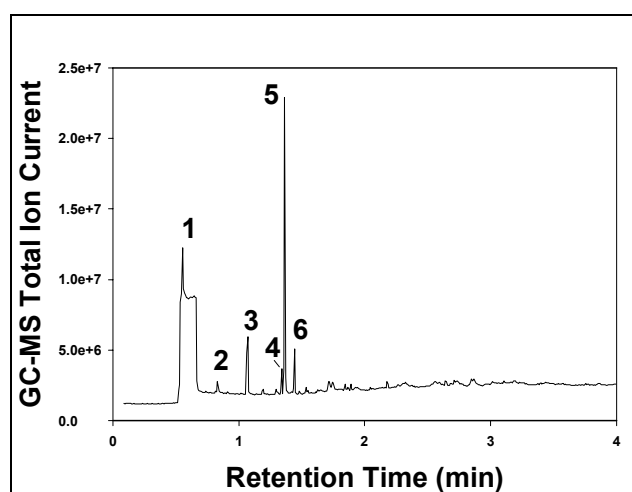
Using the optimized fiber, sampling time and temperature, good linearity was achieved on the average extracted 44 ion  $m/z$  peak area results for DIPA in Soil No. 2 from 0.7 to 3584.5  $\mu\text{g/g}$  soil ( $R^2 = 0.989$ ). It was possible to reliably quantitate DIPA in soil down to 7.2  $\mu\text{g/g}$  soil using 5 min sampling and full scan analysis. The signal to noise ( $s/n$ ) ratio was approaching 3:1 by 0.7  $\mu\text{g/g}$  soil, and the method failed to detect DIPA at 0.18  $\mu\text{g/g}$  soil. By SIM, the  $s/n$  ratio was approaching 3:1 by 0.18  $\mu\text{g/g}$  soil but DIPA was reliably detected at that concentration using a 5.0 min extraction time.

### 3.5.1 Analysis of DIPA in deionized, tap, and stream water samples spiked with contaminants

DIPA was successfully detected with 5.0 min sampling in DI, stream, and tap water at a 17.9  $\mu\text{g/mL}$  concentration level with both the benchtop and mobile GC-MS. The extracted 44 ion  $m/z$  peak areas for DI and stream water were not significantly different from each other, but the tap water sample peak area was significantly higher in response compared to the other water types. For tap water,  $p$  equaled 0.045 by One-Way ANOVA and Tukey's Post Hoc Analysis.

Next, DI, stream, and tap water samples of 17.9  $\mu\text{g/mL}$  DIPA that were spiked with 2.2  $\mu\text{g}$  BTEX/mL were analyzed on the benchtop and mobile GC-MS. Using the oven ramping parameters described previously, benzene co-eluted with DIPA. After changing the method (15  $^{\circ}\text{C/min}$  vice 25  $^{\circ}\text{C/min}$ ), benzene and DIPA were partially resolved. Similarly, benzene co-eluted with DIPA on the flash GC-MS. The results as compared by One Way ANOVA for the Mobile Van GC-MS showed that stream and DI

water were not significantly different from each other, regardless of the addition of BTEX ( $p = 0.44$ ). On both instruments, stream and DI water samples spiked with BTEX had significantly lower extracted DIPA peak area counts compared with tap water ( $p = 0.042$ ), possibly due to residual water treatment chemicals in the tap water. A typical chromatogram from the Mobile Laboratory with a flash GC-MS chromatogram of DIPA in stream water with BTEX is shown as Figure 4-3. A typical chromatogram from the benchtop GC-MS of DIPA in DI water with BTEX is shown in Figure 4-4.

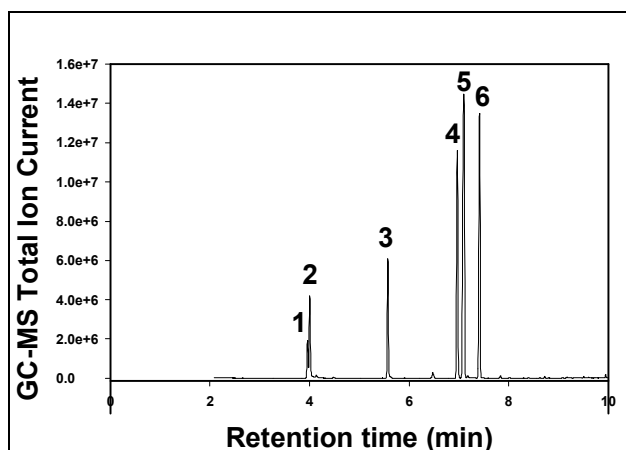


**Figure 4-3.** GC-MS chromatogram for 17.9  $\mu\text{g/mL}$  aqueous DIPA + 2.2  $\mu\text{g/mL}$  BTEX, manual headspace sampling for stream water, analyzed using van-mounted GC-MS under field conditions (PDMS DVB, 70  $^{\circ}\text{C}$ , 5 min extraction).

Compound key: **1** water<sup>1</sup>, **2** DIPA<sup>2</sup>, **3** toluene<sup>2</sup>, **4** ethylbenzene<sup>2</sup>, **5** m, p-xylene<sup>2</sup>, **6** o-xylene<sup>2</sup>.

<sup>1</sup>Identification based upon EI spectrum match.

<sup>2</sup>Identification based upon EI spectrum and retention time match with authentic standard.



**Figure 4-4.** GC-MS chromatogram for 17.9  $\mu\text{g/mL}$  aqueous DIPA + 2.2  $\mu\text{g/mL}$  BTEX, automated headspace sampling for DI water, analyzed using laboratory GC-MS (PDMS DVB, 70  $^{\circ}\text{C}$ , 5.0 min extraction). Note: 2 min solvent delay (MS off).

Compound key: 1 benzene<sup>2</sup>, 2 DIPA<sup>2</sup>, 3 toluene<sup>2</sup>, 4 ethylbenzene<sup>2</sup>, 5 m, p-xylene<sup>2</sup>, 6 o-xylene<sup>2</sup>.

<sup>1</sup>Identification based upon EI spectrum match.

<sup>2</sup>Identification based upon EI spectrum and retention time match with authentic standard.

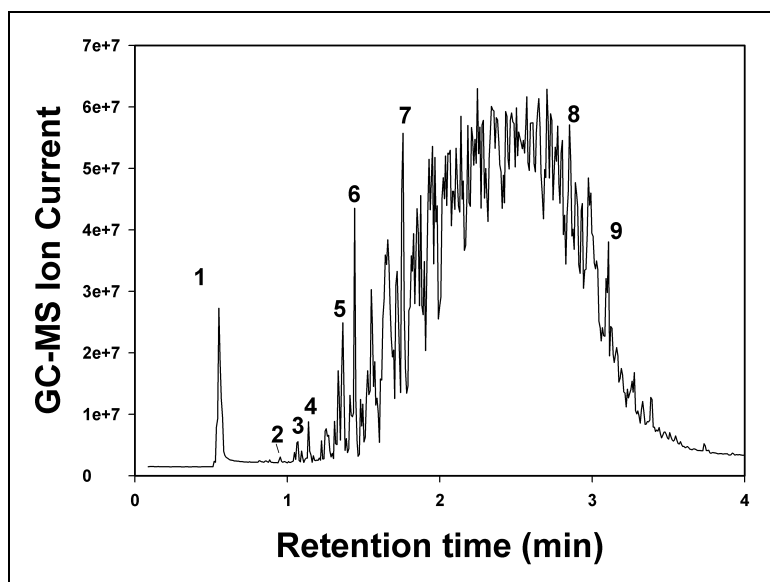
### 3.5.2 Analysis of DIPA in 3 common agricultural soil samples spiked with contaminants

Sampling 3 common agricultural soil types for 5.0 min at 30  $^{\circ}\text{C}$  for 0.72 to 3584.5  $\mu\text{g/g}$  soil gave linear correlations for DIPA peak area plotted against concentration (sandy clay loam,  $R^2 = 1.000$ ). The 3 soil types had significant differences in extracted 44 ion  $m/z$  peak areas ( $p = 0.003$ ), with the greatest peak areas occurring with the sandy loam soil due to the high silica and low organic content of that soil. The results are provided in Table 4-2. The GC-MS was overloaded with DIPA when sampling sandy loam spiked above 716.9  $\mu\text{g/g}$  soil, so the comparisons were made at this lower concentration range. There is a negative correlation, as expected, between the percentage of organic matter in the soil and the extracted 44 ion  $m/z$  peak area response.

**Table 4-2.** Comparison of benchtop GC-MS extracted 44 ion  $m/z$  DIPA peak area counts for various soil sample types (5.0 min extraction time, PDMS/DVB SPME fiber, 30 °C).

	<b>Soil Types</b>		
	<b>1</b>	<b>2</b>	<b>3</b>
<b>1</b>	$1.51 \cdot 10^8$	$1.30 \cdot 10^8$	$1.33 \cdot 10^8$
<b>2</b>	$1.49 \cdot 10^8$	$1.32 \cdot 10^8$	$1.26 \cdot 10^8$
<b>3</b>	$1.41 \cdot 10^8$	$1.37 \cdot 10^8$	$1.29 \cdot 10^8$
<b>Mean</b>	$1.47 \cdot 10^8$	$1.33 \cdot 10^8$	$1.30 \cdot 10^8$
<b><sup>1</sup>SD</b>	$5.09 \cdot 10^6$	$3.35 \cdot 10^6$	$3.50 \cdot 10^6$
<b><sup>2</sup>RSD%</b>	3.46	2.52	2.67
<b>Notes:</b>			
1 = Standard Deviation			
2 = Relative Standard Deviation %			
<b>Key:</b>			
Soil 1 = Sandy Loam			
Soil 2 = Sandy Clay Loam			
Soil 3 = Loam			

The method was successfully field tested with a common hydrocarbon contaminant in 3 agricultural soil types and is applicable for detection of DIPA and other volatile chemicals in soil. A typical chromatogram from the Mobile Laboratory with a flash GC-MS of DIPA in soil spiked with diesel fuel diluted with methanol is shown as Figure 4-5.



**Figure 4-5.** SPME/GC-MS total ion chromatogram from analysis of 35.9  $\mu\text{g}$  DIPA/g + 852.9  $\mu\text{g}$  diesel/g sandy clay loam soil, manual headspace SPME sampling, analyzed using van-mounted flash GC-MS under field conditions (5.0 min extraction, PDMS/DVB, 70  $^{\circ}\text{C}$ ).

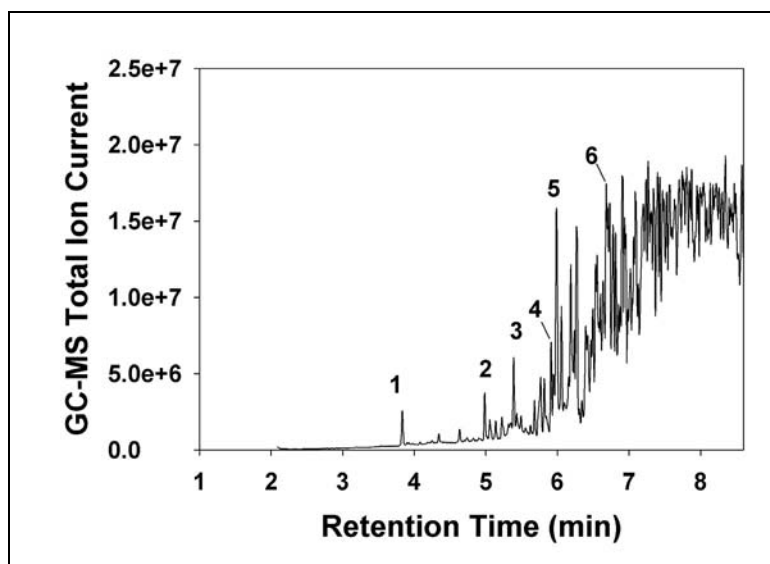
Compound key: **1** methanol<sup>2</sup>, **2** DIPA<sup>2</sup>, **3** toluene<sup>2</sup>, **4** dodecane<sup>1</sup>, **5** m, p-xylene<sup>2</sup>, **6** o-xylene<sup>2</sup>, **7** 1,2,3 trimethylbenzene<sup>2</sup>, **8** tetradecane<sup>1</sup>, **9** pentadecane<sup>1</sup>.

<sup>1</sup>Identification based upon EI spectrum match.

<sup>2</sup>Identification based upon EI spectrum and retention time match with authentic standard.

Sandy clay loam spiked with DIPA at 3584.5 and 716.9  $\mu\text{g/g}$  soil and with diesel fuel diluted with methanol (852.9  $\mu\text{g/g}$  soil) showed an average 58% and 72%, respectively, decreased 44 ion  $m/z$  peak area compared to samples without diesel. The diesel fuel vapors are most likely competing for adsorption sites on the SPME fiber coating. Figure 4-6 is a chromatogram produced by the benchtop GC-MS for analysis of DIPA and diesel in sandy clay loam. Increased organic and clay content in soil and the presence of contaminants interfered and decreased the instrument and sampling technique response for DIPA as compared to samples with low concentrations of organic matter and no contaminants. The use of an absorptive fiber such as PDMS or very short sampling times (30 sec), while not providing the optimum response for DIPA uptake, would most

likely have reduced or eliminated competitive binding and thus be more usable in sampling a complex matrix.



**Figure 4-6.** SPME/GC-MS total ion chromatogram from analysis of 716.9  $\mu\text{g}$  DIPA/g + 852.9  $\mu\text{g}$  diesel/g sandy clay loam soil, automated headspace SPME sampling, analyzed using laboratory GC-MS (5.0 min extraction, PDMS/DVB, 30  $^{\circ}\text{C}$ ). Compound key: **1** methanol<sup>1</sup>, **2** DIPA<sup>2</sup>, **3** toluene<sup>2</sup>, **4** ethylbenzene<sup>2</sup>, **5** m, p-xylene<sup>2</sup>, **6** 1,2,3 trimethylbenzene<sup>2</sup>.

<sup>1</sup>Identification based upon EI spectrum match.

<sup>2</sup>Identification based upon EI spectrum and retention time match with authentic standard.

During fieldwork (Fig. 4-4), the interior of the CBIRF Mobile Laboratory was approximately 16  $^{\circ}\text{C}$ , due to the outside temperature ( $\sim 2^{\circ}\text{C}$ ). Soil samples had to be heated on a hotplate set at  $\sim 40^{\circ}\text{C}$  to drive the DIPA into the headspace; the diesel was apparent even without heating the samples.

#### 4. Conclusions

A fairly rapid, solvent-free technique, based on SPME-GC-MS sampling, proved effective for detecting diisopropylamine in the headspace above water and soil samples. The 65  $\mu\text{m}$  PDMS/DVB SPME fiber was successful for DIPA extraction and detection with a DB-1 column in a 6890 GC-MS. Employing 5.0 min sampling for DIPA in sandy clay loam soil at 30 °C from 0.72 - 3584.5  $\mu\text{g}$  DIPA/g soil and in DI water at 70 °C from 0.28 - 17.9  $\mu\text{g/mL}$ , linear, reliable identification of DIPA and of common hydrocarbon contaminants was obtained. Detection of DIPA at levels as low as 0.0088  $\mu\text{g/mL}$  was possible in DI water with 15.0 min SIM sampling and as low as 0.018  $\mu\text{g/mL}$  with 15.0 min full range scan GC-MS analysis. Flash GC-MS was also proven in a field setting to be effective at identification of DIPA and some common hydrocarbon contaminants in soil and water. With the goal of field sampling in mind, the techniques used to optimize extraction conditions were limited to heating and stirring. This method for sample preparation, analyte extraction, and GC-MS parameters is suitable for initial onsite analysis of soil and water and for site investigation of potential chemical warfare agent production facilities by mobile forces in the field that are equipped with a GC-MS.

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## CHAPTER 5

### NOVEL APPLICATION OF A SOLID PHASE MICROEXTRACTION NEEDLETRAP WITH FAST GAS CHROMATOGRAPHY-MASS SPECTROMETRY

Douglas K. Parrish, Ingo Christ, Gary Hook

#### **Abstract**

Comparisons were made between sampling diisopropylamine (DIPA) and dimethyl methylphosphonate (DMMP) by dynamic sampling with a solid phase dynamic extraction (SPDE) needletrap device and passive sampling by solid phase microextraction (SPME) fiber with analysis by fast gas chromatography-mass spectrometry. Equilibrium vapor sampling by SPDE for DIPA (1 min. extraction, 0.036-716.9 mg/m<sup>3</sup>) and DMMP (5 min. extraction, 0.058-1150.0 mg/m<sup>3</sup>) provided linear results that achieved lower apparent limits of detection and gave significantly larger extracted ion peak areas than comparable SPME sampling. The SPDE was equipped with a small pumping device for air sampling and has shown potential for further laboratory and field use. SPDE is a dynamic sampling method having benefits similar to SPME fiber sampling with the additional benefit of increased mechanical strength and equivalent or better limits of detection and sensitivity compared to commercial SPME fibers.

*Keywords:* solid phase dynamic extraction, SPDE, fast GC, DMMP, DIPA, SPME

## 1. Introduction

### *1.1 Background*

Solid phase microextraction (SPME), when combined with gas chromatography-mass spectrometry (GC-MS) analysis, has been shown to be adaptable to sampling of a wide variety of chemicals [1-5], including chemical warfare agents (CWAs) in a field setting [6, 7]. Pawliszyn has provided a detailed discussion of SPME theory and use [8, 9].

Needletrap devices may use a syringe barrel or needle coated with a SPME polymer [10-12] or other sorbent material or may be formed around a piece of chromatographic column [12-14]. Sections of stainless steel capillary columns have been applied for the extraction of pesticides in water with analysis by GC-electron capture detection and nitrogen phosphorus detection [10]. A section of fused silica capillary GC column with Omegawax 250 stationary phase was housed in a needle and used for the direct immersion, repeated aspiration sampling of pesticides in water with analysis by high pressure liquid chromatography by Eisert and Pawliszyn [13]. Needletrap devices have also been fitted with Porapak for aqueous sampling [15] and with quartz wool for airborne particulates and aerosols [16]. The potential advantages of such a needletrap device over a typical SPME fiber would be greater mechanical durability of the phase since it is enclosed, a greater phase volume, and hence greater sensitivity and increased extraction speed [10].

The ChromSys (Alexandria, VA) solid phase dynamic extraction (SPDE) needletrap devices (also called “the magic needle”) are produced by coating the inside of a 0.8 mm needle (O.D.) with a SPME polymer instead of using a piece of

chromatographic column [10,11]. The ChromSys SPDE has been successfully used in laboratories in an automated CombiPAL system for direct immersion and headspace sampling. However, specialized automated sampling equipment was required in previous research as the best results were obtained when multiple extractions were made within a single sample [10,11].

As discussed by Smith et al. [17], a portable GC-MS such as the Inficon Hapsite (Syracuse, NY) or other detection instrumentation can be utilized downrange in the hot zone. Also, detection can be accomplished onsite outside of the contamination zone, in a warm or cold zone. With the latter in mind, the SPDE could be used for both sampling with immediate detection onsite, or could be capped, refrigerated to prevent the loss of analytes, and taken to a nearby laboratory for analysis. Smith et al. mentioned a number of desirable attributes of a field sampler: small size, ease of field use and transportation, sample concentration for trace analytes, and ability to readily introduce the sample into the GC-MS for field analysis [17].

GC-MS instruments provide the ability to identify unknown chemicals because a GC-MS can provide detailed information about a chemical's structure. Fast or flash GC-MS can provide quicker identification of chemicals by the use of a modified GC column and oven door as compared to a standard GC-MS, while still maintaining adequate resolution [18]. Advantages of a resistively heated, low-thermal mass (LTM) analytical column in flash GC-MS field-portable instruments have been well discussed [17, 19].

The desire for field sampling and onsite identification of potentially hazardous chemicals has been discussed in detail [17, 19-21]. The use of field detection methodologies such as SPME-GC-MS can provide rapid sampling, detection, and

identification of toxic industrial chemicals (TICs) and chemical warfare agents including precursors, degradants, and the neat agents themselves. The onsite commander can use the information gathered from field sampling and identification for both immediate threat detection and health risk assessment [17].

### *1.2 Current research*

The use of GC-MS has been well characterized for CWA identification but not for most precursors [22-24]. Diisopropylamine (DIPA) is an intermediate precursor for the production of the organophosphorus nerve agent *O*-ethyl *S*-(2-diisopropylaminoethyl) methylphosphonothiolate (VX) and certain pesticides and is a chlorination decontamination product of VX [25-28]. Dimethyl methylphosphonate (DMMP), used commercially in organic synthesis, is a G agent precursor [28,29].

Rasmussen et al. employed hollow fiber-based liquid phase microextraction for extraction of environmental pollutants and pharmaceutical products from liquid samples, with analysis by GC-MS and liquid chromatography-mass spectrometry (LC-MS) [30]. Lipinski published the first paper on SPDE, employing automated sampling using the ChromSys solid phase microextraction device for organic compounds in water [10]. Mushoff et al. have used SPDE for automated headspace sampling of drugs in hair samples with analysis by GC-MS [11,31]. Bicchi et al. used SPDE-GC-MS for automated sampling and detection of volatile compounds in the headspace above plants and food [32]. Others have used similar needletrap devices and syringe barrel coatings coated with SPME polymers for the concentration of organic vapors in tobacco smoke [33] as well as particulates in diesel engine exhaust [16].

In addition to detection of CWAs and their degradants by GC-MS, LC-MS, and other methods have been employed, many of which are compatible with SPME and SPDE (34-37). Cheicante et al. developed an innovative micellar electrokinetic chromatography (MEKC) technique for nerve agent identification in aqueous samples [34]. GC  $\times$  GC-Time of Flight MS [35] and LC-MS [36] have been used for DMMP detection. Similar compounds are routinely detected by GC-MS [22] and microcolumn liquid chromatography and capillary electrophoresis with flame photometric detection [37].

This research examined a commercial polydimethylsiloxane polymer with 10% activated charcoal (PDMS-AC) solid phase dynamic extraction needletrap device. Sample adsorption was performed by using a small air sampling pump to draw the air mixture through the needletrap. Analyte desorption into the GC injector was performed manually. The goal was to determine the efficacy of SPDE using a system that can be employed for field sampling in extracting and concentrating DMMP and DIPA individually in air samples without further sample preparation. Dynamic extraction has been proven to provide increased sensitivity, but requires the use of a special sampling block or chamber for commercial SPME fibers [38,39].

If these SPDE needletrap devices are shown to have increased sensitivity as compared to commercial SPME fibers, the SPDE may supplement or partially replace currently existing SPME fibers for some uses. This research sought to determine the potential for use of SPDE for vapor sampling in fieldwork with detection by GC-MS. The specific methodology employed was based on coupling a SPDE needletrap device to a handheld air sampling pump, bypassing the previous use of automated aspirations and



specialized GC inlets and plumbing. A comparison was made between SPDE and a commercial SPME fiber for extracted ion peak areas for vapor sampling of 2 CWA precursors. Successful development of a methodology based on this approach could prove useful for field detection by headspace sampling for a variety of chemicals including CWAs and their precursors.

### *1.3 Chemical information*

#### *1.3.1 Diisopropylamine*

Diisopropylamine (N-(1-methylethyl)-2-propanamine or DIPA) is produced by reaction of ammonia with isopropyl alcohol or isopropyl chloride. DIPA is an eye, respiratory, and skin irritant. In humans, symptoms of DIPA exposure can range from nausea (low concentration) to pulmonary edema and burns (high concentration) [27]. DIPA is a chlorination decontamination product of VX [25]. DIPA is used as a chemical intermediate in the synthesis of pesticides (diallate, fenamiphos), chemical warfare agents (VX), and pharmaceuticals (vitamin B-15 and anti-hypertensives). DIPA is also used as a stabilizer for mesityl oxide [27]. DIPA is not regulated by the U.S. Environmental Protection Agency (EPA). The Occupational Safety and Health Administration (OSHA) has assigned DIPA an Immediately Dangerous to Life and Health (IDLH) limit of 200 ppm (842 mg/ m<sup>3</sup>), a permissible exposure limit (PEL) of 5 ppm (20 mg/m<sup>3</sup>), and given it a skin designation indicating the potential for a high level of absorption through skin [27].

### *1.3.2 Dimethyl methylphosphonate*

Dimethyl methylphosphonate (DMMP) is a common industrial solvent and additive used in the manufacture of plastics, the extraction of heavy metals, and the production of phosphorus-based nerve agents [28, 29]. DMMP has been shown to cause muscle weakness, respiratory depression, and decreased fertility in rats, but there is no direct human health data. The EPA Health Advisory for DMMP in drinking water is a maximum of 100 µg/L [29]. OSHA does not currently regulate DMMP exposure.

## **2. Materials and methods**

### *2.1 Materials*

DMMP, DIPA, methanol, and benzene, toluene, ethylbenzene, and xylenes (BTEX) were purchased from Sigma Aldrich (Milwaukee, WI, USA). Tedlar bags (3.0 L, SKC, Eighty Four, PA, USA) were used for preparing samples. CAR/PDMS fibers and holders are commercially available from Supelco (Bellefonte, PA, USA). SPDE needletrap devices are commercially available from ChromSys (Alexandria, VA, USA).

### *2.2 GC-MS methods*

A Viking Portable Spectra-Trak 573 (Bruker-Daltonics, Billerica, MA, USA) portable GC-MS was employed (Figure 5-1). The GC was retrofitted with a fast GC, Low Thermal Mass A68 door unit (RVM Scientific, Santa Barbara, CA, USA) with a DB-5MS (J&W Scientific, Folsom, CA, USA), 30 m × 0.25 mm I.D. column having a film thickness of 0.25 µm. Helium carrier gas was provided at a constant head pressure of 17 psi. A 0.75 mm (for SPME) or a 1.5 mm (for SPDE) I.D. deactivated injection port liner

(Supelco) was used to rapidly transfer desorbed analytes onto the front of the column. The Viking has a universal inlet septum, but other GC inlets such as the Agilent 6890 (Wilmington, DE, USA) require the use of a modified septum nut (ChromSys). The GC oven was held constant at 250 °C while the RVM column was programmed to start at 40 °C, ramp at 150 °C per min to 250 °C, and hold there for 96 sec. Desorption of the SPME fiber samples and injection of the SPDE were accomplished in the splitless injection mode for 2.0 min, followed by 40 mL/min injector purge. The injector and MS transfer line temperatures were held constant at 250 °C. Electron impact ionization (70 eV) was used and mass spectra were collected over the range of 10-300 mass to charge ( $m/z$ ). Sample retention characteristics and mass spectra were stored using the HP Chemstation software package.



**Figure 5-1.** Viking GC-MS with flash GC (externally mounted).

### *2.3 Solid Phase Microextraction (SPME)*

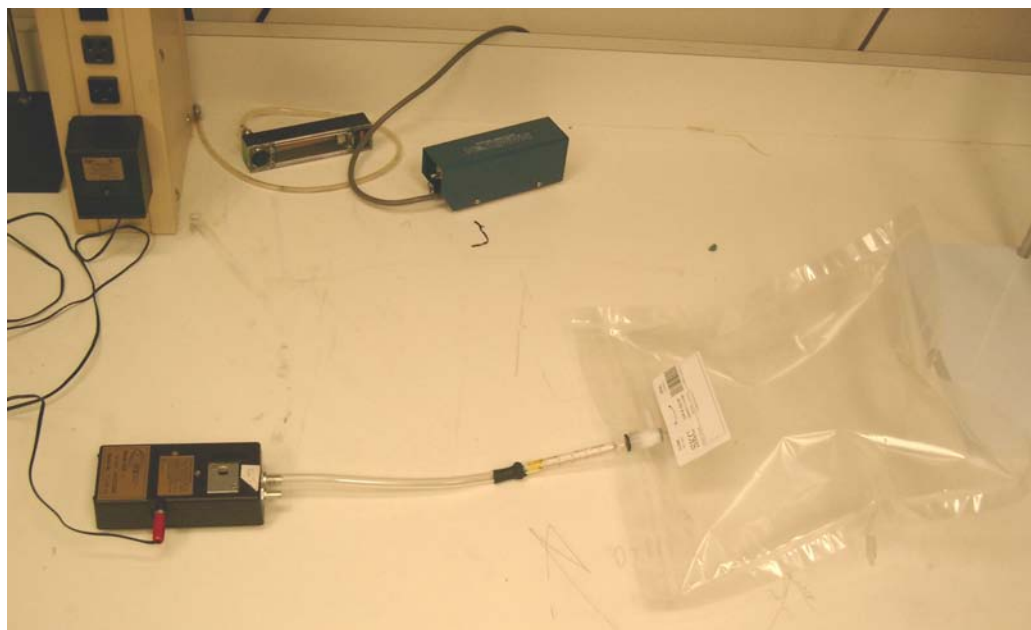
The 85  $\mu\text{m}$  Carboxen/polydimethylsiloxane (CAR/PDMS) SPME fiber for this research was selected due to its similarity to the PDMS/10% AC SPDE needletrap. A manual fiber holder was used to introduce the fiber into the Tedlar bag via the septum and then into the GC injection port immediately after sampling.

### *2.4 Solid Phase Dynamic Extraction (SPDE)*

The SPDE was a 50  $\mu\text{m}$  thick PDMS with 10% activated charcoal (PDMS-AC) coating on the inside of a 50 mm stainless steel needle (0.5 mm  $\pm$  0.1 mm I.D. with a conical needle tip having a 0.4 mm<sup>2</sup> side port). The hole at the top of the 2.5 mL gas tight glass syringe, normally used in autosampling for gas flushing, was sealed for these experiments. The air sampling pump used for all initial experiments was an SKC Model 222-3 (Eighty Four, PA, USA) industrial hygiene personal sampling pump, run directly from 120VAC electrical power. The pump was connected to the SPDE with Tygon and butyl rubber tubing. A smaller, battery operated air pump, the PAS 500 (Field Forensics, St Petersburg, FL, USA) was used in a final experiment to determine if a smaller pump was effective. Both air pumps were calibrated to 0.15 LPM with a Bios DryCal DC-Lite (Butler, NJ, USA) primary flow meter.

The SPDE was inserted into the Tedlar bag via the septum (Figure 5-2), and the sampling was performed. Upon completion of the sampling, the needle was removed from the bag and the plunger was re-installed. The needle was then immediately placed into the GC injection port where the SPDE was allowed to heat for 30 sec. At this point the plunger was drawn up to fill the syringe with 0.5 mL of helium carrier gas. The

plunger was then manually depressed at approximately 0.05 mL per second. Initial aspiration plunger speed, flush gas volume for desorption, and needle-preheat time were based on the research of Lipinski [10], Mushoff et al. [11,31], and Bicchi et al. [32] and modified as required. The SPDE was completely desorbed by placing it into a syringe cleaner (Hamilton, Reno, NV) and blowing ambient air across the heated needle interior for 5 min with an SKC personal sampling pump. Unlike with the use of an autosampler by Mushoff [11, 31] and Lipinski [10] which supplied carrier gas, a single preheat and manual injection of the SPDE into the injection port did not fully desorb the analytes, thus requiring the use of a syringe cleaner or similar device. Total desorption was possible by multiple injections of the heated SPDE needle in the GC injection port for 10 min but was not as efficient as the use of a syringe cleaner.



**Figure 5-2.** SKC sampling pump and SPDE (needle cleaner in the background).

## *2.5 Sample preparation*

Tedlar bags (3.0 L) were purged with nitrogen, filled with ambient air via a 2.0 L syringe (SKC, Inc), and then injected with neat or dilute analyte. Each sample was allowed to equilibrate for 5.0 min prior to sampling.

## *2.6 Method optimization*

### *2.6.1 Selection of optimal sampling time*

Uptake curves were developed by separate analysis of DMMP (1150.0 mg/m<sup>3</sup>) and DIPA (716.9 mg/m<sup>3</sup>) air samples in 3.0 L Tedlar bags. Triplicate samples were collected for 0.25, 0.5, 1, 5, and 10 min for SPDE for both chemicals, in separate bags. All measurements were performed at laboratory ambient temperatures (23 – 24 °C).

### *2.7 Exploring the apparent limits of detection of DMMP and DIPA*

Sensitivity was determined using the optimized sampling time, ambient temperature, and full range MS scan. Sampling was attempted for 0.018 to 716.9 mg/m<sup>3</sup> for DIPA and 0.029 to 1150.0 mg/m<sup>3</sup> for DMMP. The apparent limits of detection (> 3:1 signal to noise or *s/n* ratio compared to background) were obtained with the optimized extraction time.

### *2.8 Analysis of air samples of DMMP and DIPA with hydrocarbon-contamination*

Hydrocarbon contaminants (10 ppm BTEX) which can be representative of environmental samples were used to challenge the methodology for both SPME and SPDE by spiking these contaminants during initial sample preparation. The SKC and PAS500 (Figure 5-3) sampling pumps were both used for this test.



**Figure 5-3.** PAS500 with SPDE and SPME

## 2.9 Statistical Methods

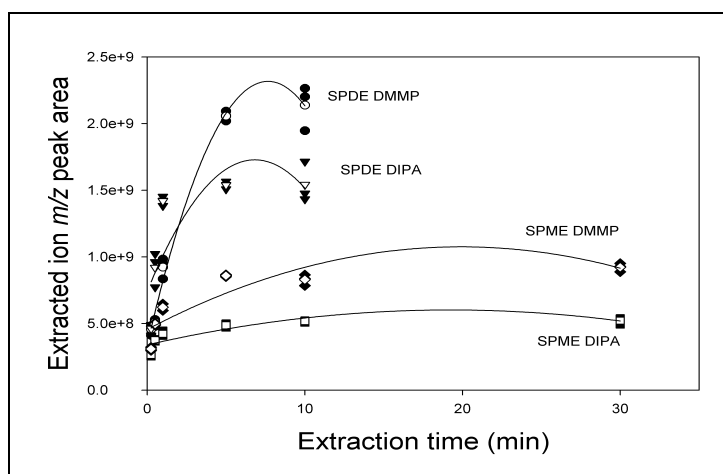
Experimental data was examined for differences between chemical-specific ion  $m/z$  peak areas. To examine reproducibility, the samples were run in triplicate and relative standard deviations (RSD) calculated. One-Way Analysis of Variance (ANOVA) was used to compare the extracted ion  $m/z$  peak area results for each chemical to determine the optimum extraction time, followed by Tukey's post hoc comparison to examine the source of variance. SPDE was compared to SPME for each chemical's peak area at all concentrations (using the optimal extraction time) with Two-Way ANOVA. Descriptive statistics were used in the analysis of data, including the variance and linear regression characteristics. Microsoft Excel 2000 (Version 9.0.2720) was used to perform RSD calculations, and SPSS Version 11.0.1 provided linear regression analysis.

### 3. Results and discussion

#### 3.1 Sampling time selection

SPDE approached equilibrium significantly quicker than SPME for DIPA and at the same time for DMMP. The dynamic sampling of SPDE has been shown by others to achieve significantly faster extraction speeds than passive SPME sampling due to the increased movement of vapor phase analytes and the increased phase surface area associated with SPDE [10,11,32]. The PDMS-AC SPDE has a phase volume of approximately  $4.40 \text{ mm}^3$  [11] while the Supelco  $85 \text{ }\mu\text{m}$  CAR/PDMS StableFlex fiber has a phase volume of  $0.528 \text{ mm}^3$ .

Figure 5-4 shows the uptake curves for DMMP and DIPA obtained with SPDE and SPME. Using SPDE, DIPA apparently reached equilibrium by 1.0 min. The DIPA peak area obtained by 1.0 min sampling SPDE was not significantly different than 5.0 and 10.0 min sampling ( $p = 0.56$  and  $1.00$ , respectively). DMMP reached equilibrium at approximately 5.0 min. The DMMP 5.0 min sampling peak area by SPME was not significantly different than 10.0 min sampling ( $p = 0.79$ ).



**Figure 5-4.** Headspace SPDE and SPME uptake curves, full scan GC-MS 44 and 79  $m/z$  extracted ion current average peak areas for  $716.9 \text{ mg/m}^3$  DIPA and  $1150 \text{ mg/m}^3$  DMMP, respectively, plotted against SPME sampling time.



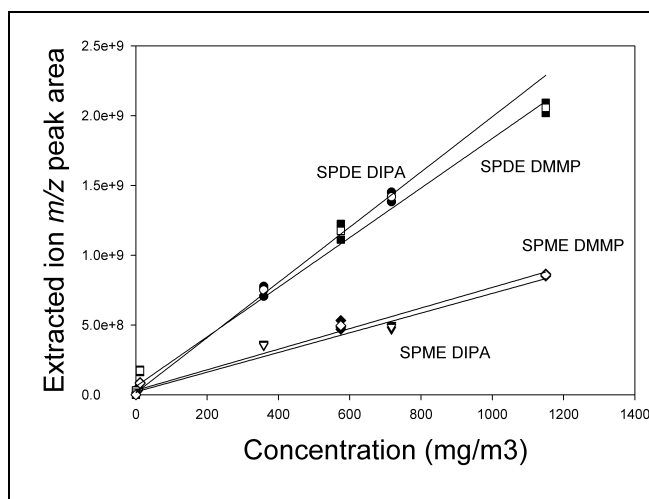
Using SPME, DIPA apparently reached equilibrium at approximately 5.0 min. The DIPA peak area obtained by 5.0 min sampling SPDE was not significantly different than 10.0 and 30.0 min sampling ( $p = 0.28$  and  $0.20$ , respectively). DMMP reached equilibrium at approximately 5.0 min. The DMMP 5.0 min sampling peak area by SPME was not significantly different than 10.0 or 30.0 min sampling ( $p = 0.65$  and  $0.08$ , respectively).

### *3.2 Exploring the apparent limits of detection of DMMP and DIPA*

SPDE gave better limits of detection than SPME for both chemicals sampled. Sensitivity was determined using the optimized sampling time, ambient temperature, and full range MS scan. SPDE gave linear results for DIPA (1 min sampling from  $0.036$  to  $716.9 \text{ mg/m}^3$ ,  $R^2 = 0.999$ ) and DMMP (5 min sampling from  $0.058$  to  $1150.0 \text{ mg/m}^3$ ,  $R^2 = 0.996$ ). SPME also gave linear results for DIPA (5 min sampling from  $0.072$  to  $716.9 \text{ mg/m}^3$ ,  $R^2 = 0.954$ ) and DMMP (5 min sampling from  $0.12$  to  $1150.0 \text{ mg/m}^3$ ,  $R^2 = 0.992$ ). SPDE gave a lower apparent limit of detection (LOD) for DIPA than did SPME,  $0.036$  and  $0.072 \text{ mg/m}^3$ , respectively (Figure 5-5). For DMMP, SPDE gave a lower level of detection,  $0.058$  compared to  $0.12 \text{ mg/m}^3$ .

For all concentrations on both chemicals, SPDE gave significantly higher peak areas than did SPME ( $p = 0.000$  for concentration and method). This is most likely due to the increased phase and adsorptive capacity of SPDE, resulting in larger peak areas. There is a significant difference in peak area based on extraction method as demonstrated by Two-Way ANOVA. The residuals are not normally distributed but are not highly skewed, so normality was assumed to hold true. ANOVA is not the ideal statistical tool under these conditions; however, transformation of the peak area data was not required

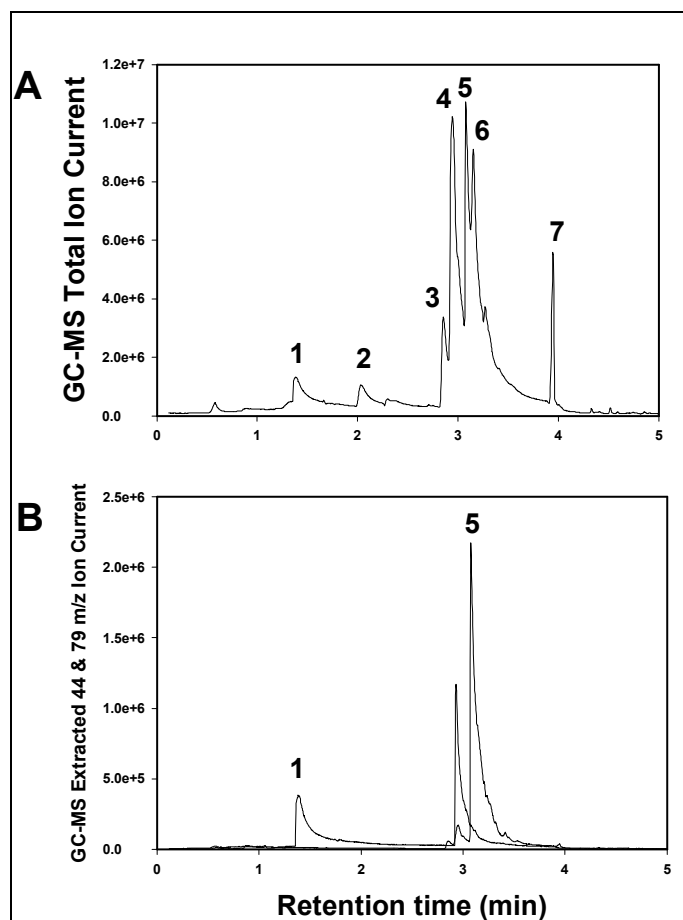
because the robustness of the ANOVA method enables it to handle small violations like those found in this data set.



**Figure 5-5.** Headspace SPDE and SPME apparent LOD curves, full scan GC-MS 44 and 79  $m/z$  extracted ion current average peak areas for 0.04 - 716.9  $\text{mg}/\text{m}^3$  DIPA (1 min sampling by SPDE, 5 min by SPME) and 0.06 - 1150.0  $\text{mg}/\text{m}^3$  DMMP (5 min sampling, SPDE and SPME), respectively, plotted against SPME sampling time.

### 3.3 Analysis of air samples of DMMP and DIPA with hydrocarbon-contamination

Possible low level hydrocarbon contaminants (10 ppm BTEX), DMMP, and DIPA were successfully identified by both SPDE (Figure 5-6) and SPME (Figure 5-7). A second, smaller battery-powered sampling pump was also tested. The SKC and PAS500 sampling pumps gave similar results. In order to improve the resolution of some of the isomers in BTEX, it was necessary to slow the RVM ramp down to 40 °C for 5 sec, then 20 °C/min to 180 °C, and held for 55 sec.

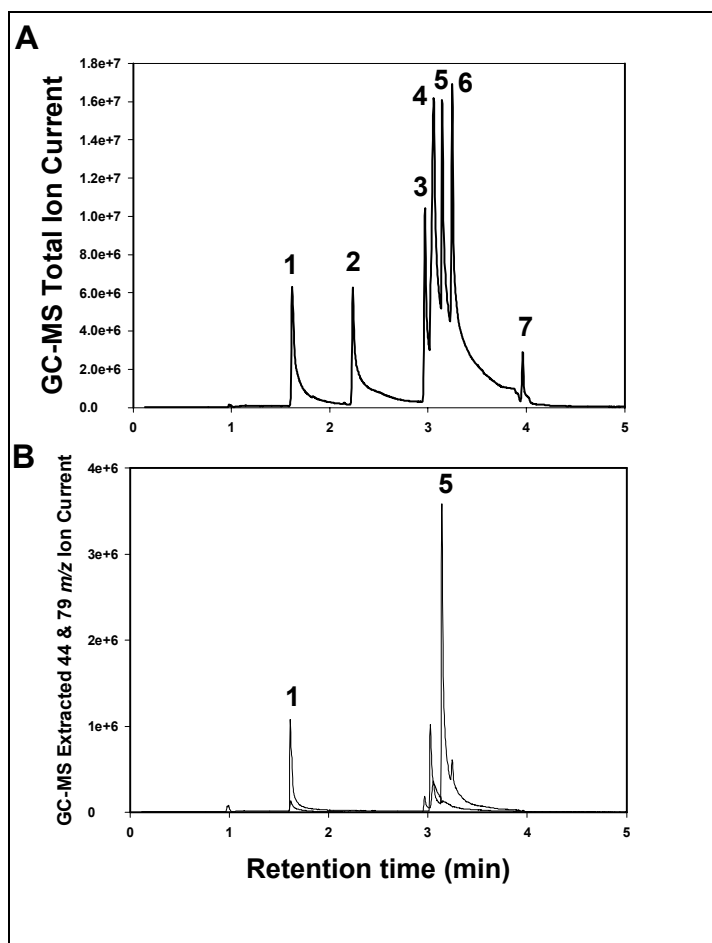


**Figure 5-6A.** SPDE/fast GC-MS chromatogram for 11.5 mg/m<sup>3</sup> DMMP, 7.2 mg/m<sup>3</sup> DIPA, 10 mg/m<sup>3</sup> BTEX, SPDE sampling with an SKC small air pump (PDMS-AC, 23 °C, 5 min extraction).

**Figure 5-6B.** SPDE/fast GC-MS 44 and 79 *m/z* extracted ion chromatograms overlaid for 11.5 mg/m<sup>3</sup> DMMP, 7.2 mg/m<sup>3</sup> DIPA, 10 mg/m<sup>3</sup> BTEX, SPDE sampling with an SKC small air pump (PDMS-AC, 23 °C, 5 min extraction).

Compound key: **1** benzene and DIPA co-elute<sup>2</sup>, **2** toluene<sup>2</sup>, **3** ethylbenzene<sup>2</sup>, **4** m-, p-xylenes<sup>2</sup>, **5** DMMP<sup>2</sup>, **6** o-xylene<sup>2</sup>, **7** phenol<sup>1</sup>.

<sup>1</sup>Identification based upon EI spectrum match.



**Figure 5-7A.** SPME/fast GC-MS chromatogram for 11.5 mg/m<sup>3</sup> DMMP, 7.2 mg/m<sup>3</sup> DIPA, 10 mg/m<sup>3</sup> BTEX (CAR/PDMS, 23 °C, 5 min extraction).

**Figure 5-7B.** SPME/fast GC-MS 44 and 79 *m/z* extracted ion chromatograms for 11.5 mg/m<sup>3</sup> DMMP, 7.2 mg/m<sup>3</sup> DIPA, 10 mg/m<sup>3</sup> BTEX, manual headspace SPME sampling (CAR/PDMS, 23 °C, 5 min extraction).

Compound key: **1** DIPA<sup>2</sup>, **5** DMMP<sup>2</sup>.

Compound key: **1** benzene and DIPA co-elute<sup>2</sup>, **2** toluene<sup>2</sup>, **3** ethylbenzene<sup>2</sup>, **4** m-, p-xylenes<sup>2</sup>, **5** DMMP<sup>2</sup>, **6** o-xylene<sup>2</sup>, **7** phenol<sup>1</sup>.

<sup>1</sup>Identification based upon EI spectrum match.

<sup>2</sup>Identification based upon EI spectrum and retention time match with authentic standard.

#### 4. Conclusions

A method based on dynamic air sampling by a small air pump through a solid phase dynamic extraction, needle-trap device proved effective for concentrating vapor-

phase DIPA and DMMP for detection by fast GC-MS. The SPDE gave significantly increased peak areas compared to a similar SPME fiber due to active sampling and an increased phase volume. A very small, battery operated air pump was successfully used with this rugged needletrap device for dynamic sampling of a complex mixture of hydrocarbons and CWA precursors in air. Because of the increased durability inherent to the design of the SPDE and the increased sensitivity, this sampling technique has demonstrated the potential for field use for headspace sampling of various volatile chemicals, including chemical warfare agents and precursors. It is possible this SPDE methodology may supplement field use of SPME, but further investigation is required to optimize all parameters.

### **Acknowledgements**

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## CHAPTER 6

# NOVEL APPLICATION OF FAST GAS CHROMATOGRAPHY WITH QUADRUPOLE ION TRAP, TIME-OF-FLIGHT PHOTOIONIZATION MASS SPECTROMETRY

Douglas K. Parrish, Philip A. Smith, Gary L. Hook

### **Abstract**

A fast gas chromatography (GC) capillary column and injection port were interfaced with a novel quadrupole ion trap, time-of-flight photoionization mass spectrometer (Qit ToF PI-MS). Solid phase microextraction (SPME) was used to provide headspace extraction of several chemical warfare agent precursors and degradants for introduction to this GC/PI-MS. The benefits of using a soft ionization method like photoionization include non-ionization of most constituents of air and common solvents while providing minimal fragmentation of molecules of interest, leading to a cleaner chromatogram. This novel mass spectrometer detection system has potential for further laboratory and field use.

*Keywords:* QitTof, photoionization, fast GC-MS, CWA precursors

## 1. Introduction

Published methods for the identification of chemical warfare agents (CWAs) and a limited number of precursors are often based on liquid and gas chromatography. A number of detectors have been employed, including mass selective, ultraviolet, nitrogen phosphorus, and electron capture [1-3]. Gas chromatography mass spectrometry (GC-MS) with electron impact ionization is widely employed for CWA and toxic industrial chemical (TIC) detection in both field and laboratory settings [4-8]. A properly adapted GC-MS provides detailed structural and mechanistic information on analytes. Using GC-MS techniques, it is possible to identify unknown chemicals and quantify the presence of known chemicals in a variety of matrices. This equates to the ability to correctly identify precursors, CWAs, and common organic compounds in a single sample.

The ability to detect and positively identify the specific single and dual-use CWA precursors at a site is crucial in confirming that a site was used for CWA manufacture vice standard industrial operations such as pesticide production. Onsite confirmatory equipment is recommended since it gives near real-time results, greatly increasing the rapidity of health risk planning and consequence management response. Several authors have discussed the importance of a field portable GC-MS and specific, field-ready techniques including the use of solid phase microextraction (SPME) [9-11].

SPME is a generally simple, fast, and inexpensive sampling strategy that reduces or eliminates the use of solvents and cumbersome analytical steps, minimizing the waste stream and potential exposure to potentially hazardous solvents and analytes [11]. SPME, when combined with GC-MS analysis, has been shown to be adaptable to sampling of a

wide variety of chemicals [9,10,12-17]. The theoretical aspects of SPME are well defined [11,18].

Typical electron ionization (EI or electron impact ionization) MS instruments produce a relatively cluttered fragmentation pattern, performing hard ionization of volatile organic solvents and the constituents of air [19]. This fragmentation can make the identification of the specific analyte difficult, since the molecular ion may be weakly represented or absent. The benefits of EI mass spectrometry are that most chemicals are well documented with this method in standard, readily available electronic libraries.

Similar to chemical ionization, photoionization (PI) employs a soft ionization method that leaves a relatively intact molecular ion, allowing ready identification of many high molecular weight chemicals. Photoionization has the additional benefit of minimal signal from air and most solvent molecules [19]. A disadvantage is that there are relatively few electronic library entries for photoionization mass spectrometry.

Syagen Technologies, Inc (Tustin, CA) developed a novel photoionization source that allows low pressure and atmospheric pressure ionization, coupled with MS detection. The company has several systems, including time of flight (TOF) MS and sample introduction by GC, pyrolysis, and other methods [20-22]. The company is currently developing a solid phase microextraction (SPME) GC-MS system as well as a field portable unit based on APPI-MS [23]. Chemical warfare precursors and agents have been detected by direct air sampling using the Syagen PI source, coupled with a QitToF MS [20]. Limited research has also been done using a GC-QitToF PI-MS [20,24].

The Syagen, Inc. Quadrupole Ion Trap Time of Flight Photoionization Mass Spectrometer (QitToF PI-MS) instrument used in this research is a step toward the

development of a field portable instrument. Two systems developed by Syagen, Inc and others are atmospheric pressure photoionization (APPI) and low pressure photoionization (LPPI). The Syagen, Inc. LPPI source has been shown to produce a high signal to noise ratio, a detection limit in the ppb range, and high specificity for the identification of CWAs by direct air sampling. Additional benefits provided by this relatively new LPPI detection technology include increased sensitivity for the detection of CWAs as compared to many traditional systems [19,20]. An advantage to using an ambient or nearly ambient pressure device such as LPPI or APPI is the reduction in the size of the vacuum system required, equating to lower power requirements and reduced weight. For a truly man-portable GC-MS, weight and power limitations can be critical.

Borsdorf et al. have employed APPI coupled with MS-MS for detection of dihalogenated benzenes [25]. Liquid chromatography (LC) with APPI-MS has been used for detection of antibiotic residues in fish [26]. APPI-MS has also been used for on-line, near-real time detection of gaseous and particulate organic analytes [27].

The CWA precursors, degradants, and simulants chosen for study are listed in Table 6-1. These chemicals were chosen because they represent a wide range of volatilities and warfare agents.

**Table 6-1.** Selected Chemical Warfare Agent Precursors, Degradants, or Simulant

<b>Chemical</b>	<b>CAS #</b>	<b>Related CWA</b>
bis(diisopropylaminoethyl) disulfide (DES <sub>2</sub> )	65332-44-7	VX degradant [28,29]
Diethyl methylphosphonate (DEMP)	683-08-9	Precursor for nerve agents [30]; VX degradant [29]
Diisopropylamine (DIPA)	108-18-9	VX precursor, degradant [29,31,32]
Diisopropyl methylphosphonate (DIMP)	1445-75-6	GB, GD impurity [29]
Dimethyl methylphosphonate (DMMP)	756-79-6	G agent precursor and simulant [33,34]
Hydrogen cyanide	74-90-8	GA precursor, degradant [29]
Malathion	121-75-5	VX simulant
Malononitrile	109-77-3	CS teargas degradant [34]
Pinacolyl alcohol	464-07-3	GD precursor, degradant [29,33]
Thiodiglycol (TDG)	111-48-8	HD precursor, degradant [29,30]
Thionyl chloride	7719-09-7	Precursor for various nerve agents & vesicants [30,32]
Tributyl phosphate	126-73-8	Precursor for phosphorus oxychloride, a CWA precursor [30,35]
O,O'-diethyl methyl phosphonothioate	6996-81-2	VX impurity [29]

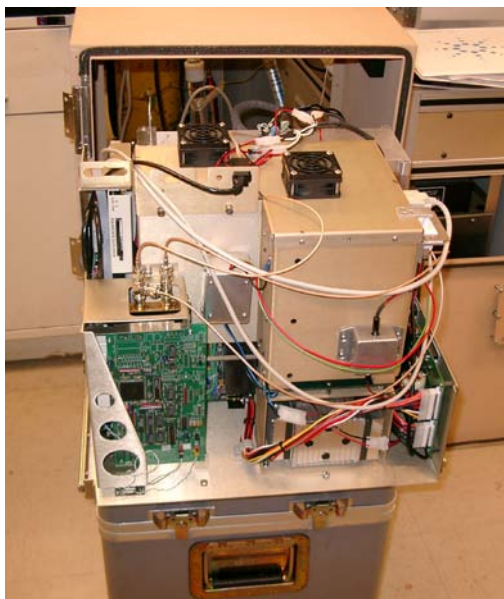
This research sought to integrate the benefits of sample concentration by SPME with a novel LPPI MS detection system for the identification of CWA precursors and common interferents. Similar systems have been proposed by Syagen, Inc. but are in initial production. At the FBI Academy, Eckenrode and Whitchurch have already displayed the ability of a Syagen Fieldmate<sup>TM</sup> with a dual EI/PI source to detect trace chemicals concentrated by SPME, employing a 6 m flash GC column mounted in the cabinet of the Syagen Fieldmate<sup>TM</sup> QitToF PI-MS [24]. The research reported here focused on further testing SPME to concentrate samples for introduction into a Syagen photoionization MS detector via a flash GC equipped with a standard 30 m column.

## 2. Experimental

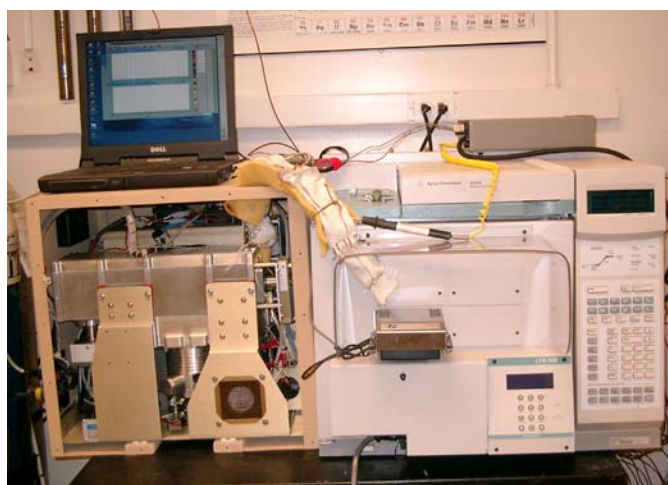
Sample vials were 20 mL silanized clear glass with 20 mm silicone-polytetrafluoroethane (PTFE) septum caps (MicroLiter Analytical Supplies, Suwanee, GA, USA). Reagent grade methanol, diisopropylamine (DIPA), dimethyl methylphosphonate (DMMP), thiodiglycol (TDG), thionyl chloride, tributyl phosphate, pinacolyl alcohol, malononitrile, diisopropyl methylphosphonate (DIMP), diethyl methylphosphonate (DEMP), malathion, potassium cyanide, and O,O'-diethyl methyl phosphonothioate, sodium sulfate, sulfuric acid, and 1L Tedlar bags were obtained from Sigma Aldrich (Milwaukee, WI, USA). Dilute bis(diisopropylaminoethyl) disulfide (DES)<sub>2</sub> was obtained from Dr. Paul Savage, University of Utah at 3.8 mg/mL.

The use of 65 µm polydimethylsiloxane/divinylbenzene (PDMS/DVB) SPME fibers follows previous work by Hook et al. [17]. PDMS/DVB fibers and holders are commercially available (Supelco, Bellefonte, PA). A manual fiber holder was used to introduce the fiber into the vial via the silicone-PTFE septum then into the GC injection port immediately after sampling.

The unmodified Syagen Inc. RadiancePro FieldMate PI-MS is shown in Figure 6-1. The PI-MS is equipped with a unique Quadrupole Ion Trap Time of Flight MS (QitTof MS), which provides extremely fast resolution and sorting of ions of analytes. Only limited publications are now emerging on the use of a QitTof PI-MS, as Syagen has only recently perfected the device [21,24]. The flash GC column modification employed in the research presented here is pictured in Figure 6-2.



**Figure 6-1.** Rear view (case off) of the Sygen Technology, Inc RadiancePro FieldMate™ Photoionization Mass Spectrometer



**Figure 6-2.** Fieldmate™ (left) connected to Agilent 6890 with modified RVM flash GC.

The injection port of a 6890 gas chromatograph (Agilent Technologies, Wilmington, DE, USA) was connected to a flash GC, Low Thermal Mass A68 door unit (RVM Scientific, Santa Barbara, CA) with a DB-5MS (J&W Scientific), 30m × 0.25 mm I.D. column having a film thickness of 0.25 μm. Helium carrier gas was provided at a

constant head pressure of 10 psi. For several initial experiments, high purity hydrogen carrier gas was produced by water electrolysis and provided at a constant head pressure of 10 psi. A 0.75 mm deactivated injection port liner (Supelco, Bellafonte, PA, USA) was used to rapidly transfer desorbed analytes onto the front of the column. The GC oven temperature was held constant at 250 °C while the RVM column was programmed to hold at 40 °C for 5 sec, ramp at 50 °C per min to 250 °C, and hold for 73 sec. The GC inlet was maintained at 250 °C. Desorption of the SPME fiber samples was accomplished in the splitless injection mode for 2.0 min, followed by 40 mL/min injector purge. The injector and MS transfer line temperatures were held constant at 250 °C. Heat rope (Eutech Instruments, Singapore) was used to heat the 0.25 mm silica transfer line (Agilent) to 150 °C, controlled by a Barnant Co (Lake Barrington, IL, USA) R/S temperature controller. The silica transfer line was routed to the Syagen MS through a 1/32<sup>nd</sup> inch Supelco Steel deactivated transfer line for mechanical support and protection. Sample retention characteristics and mass spectra were stored using the Syagen embedded software package. The operating parameters of the MS are listed in Table 6-2.

**Table 6-2.** FieldMate<sup>TM</sup> Operational Parameters

TOF Drift tube voltage	100mV
Scan rate	60 Hz/11,000 runs (3 min) or 10 Hz/2,500 runs (4.2 min), 500 megasamples per sec (MS/s)
QIT temperature	145 °C
PI source heater	185 °C
Mass range	60-335 mass to charge ( <i>m/z</i> )
Chamber pressure	$2.2 \times 10^{-5}$ torr
MS Foreline pressure	1.2 torr



Initial identification of each chemical was performed by SPME sampling above 0.5 mL of neat chemical in a 20 mL capped, silanized vial. All sampling was performed after 5.0 min temperature equilibration. DMMP was sampled at room temperature (~23 °C), TDG at 70 °C, and all other chemicals at 50 °C. DIPA, TDG, and DMMP sampling temperatures were based on preliminary PDSM-DVB SPME optimization studies. Headspace sampling for HCN was performed over 2 mL of distilled water spiked with 1.0 mg of sodium cyanide, 0.25 mL sulfuric acid, and 1.0 g sodium sulfate. In addition, serial dilutions were performed with methanol for DIPA, TDG, and DMMP, separately analyzed in capped 20 mL vials. One additional analysis was made on 1 µL each of neat DIMP, DMMP, and DEMP injected into a 1L Tedlar bag, sampled at room temperature. Analysis was attempted for 11 chemicals: thionyl chloride, tributyl phosphate, pinacolyl alcohol, malononitrile, TDG, DIMP, DMMP, DIPA, malathion, HCN, and (DES)<sub>2</sub>.

### **3. Results and Discussion**

The detection results are displayed in Table 6-3. Originally, hydrogen carrier gas was employed, but did not produce the desired sensitivity (high limits of detection, apparently because hydrogen does not cool the ions in the ion trap as required and makes a difference in the pumping speed). All subsequent research was performed with helium carrier gas at the advice of Dr. Jack Syage and Dr. Jianwei Li of Syagen Technology, Inc.

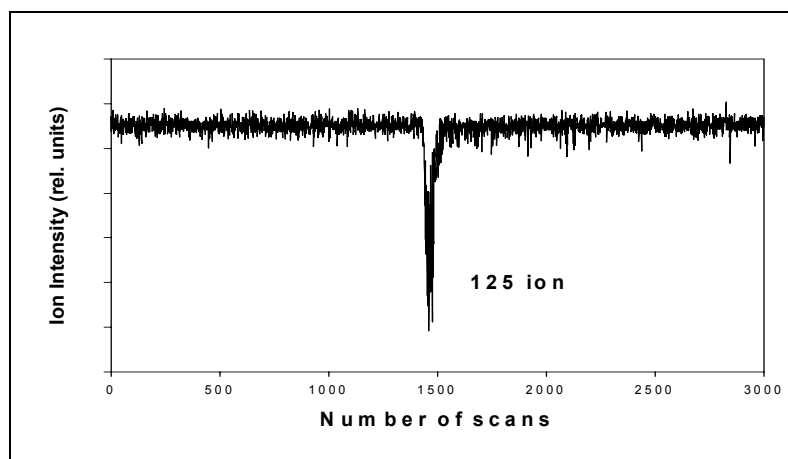
We were able to detect DMMP at levels as low as 2.9 mg/m<sup>3</sup> and DIPA as low as 35.8 mg/m<sup>3</sup> with 5.0 min sampling. The other chemicals were sampled at higher concentrations (saturated headspace) at 50 °C, with the following results. Chromatograms

are shown in Figures 6-3 to 6-9. DMMP, DEMP, and DIMP are shown, sampled together (Figure 6-10).

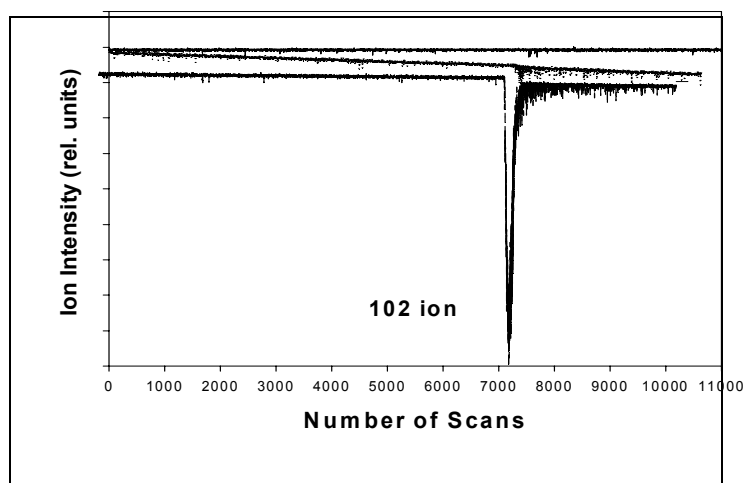
The following chemicals were not detected: tributyl phosphate, malathion, HCN, and dilute (DES)<sub>2</sub>. Using the same extraction parameters, these chemicals were detected on a flash GC-EI-MS (Viking 573, Bruker Daltonics, Billerica, MA), indicating that the extraction methodology was not a major contributor to the lack of detection. HCN was not detected because this PI-MS does not produce the required high ionization energy. The other 3 chemicals were possibly not detected due to their low volatility, relatively high molecular weight, and possible cold trapping in the transfer line from the flash GC to the PI source. The lack of sensitivity with this prototype instrumentation may have been due to cold spots in the transfer line or an incorrect software setting.

**Table 6-3.** Sampling Results.

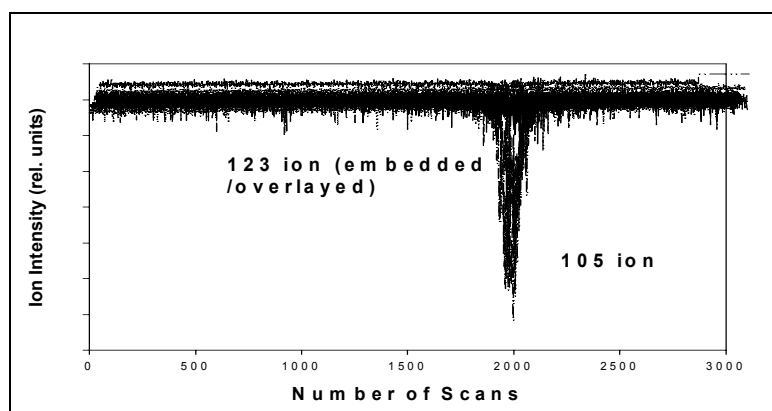
<b>Chemical</b>	<b>MW [36]</b>	<b>Detected?</b>
bis(diisopropylaminoethyl) disulfide (DES <sub>2</sub> )	320	No.
Diethyl methylphosphonate (DEMP)	152	Yes.
Diisopropylamine (DIPA)	101	Yes.
Diisopropyl methylphosphonate (DIMP)	180	Yes.
Dimethyl methylphosphonate (DMMP)	124	Yes.
Hydrogen cyanide	27	No.
Malathion	330	No.
Malononitrile	66	Yes.
Pinacolyl alcohol	102	Yes.
Thiodiglycol (TDG)	122	Yes.
Thionyl chloride	118	Yes.
Tributyl phosphate	266	No.
O,O'diethyl methyl phosphonothioate	168	Yes.



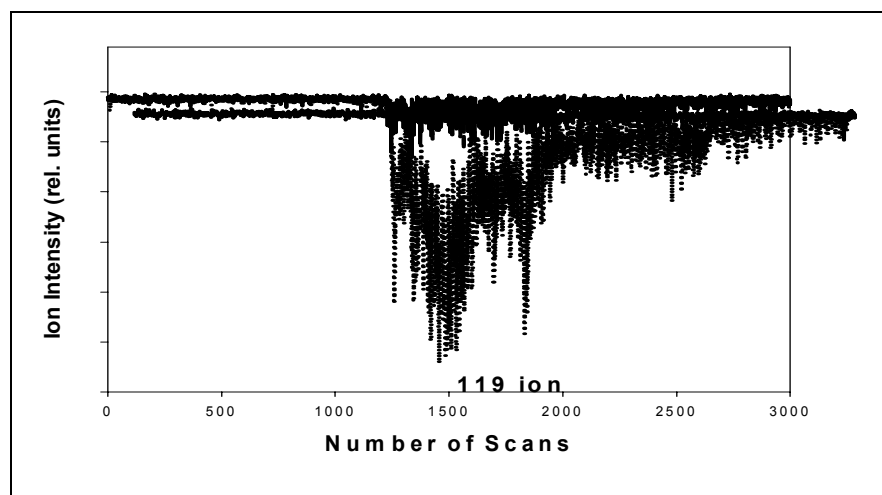
**Figure 6-3.** Headspace SPME/GC-PI-MS total ion chromatogram from analysis above neat dimethyl methyl phosphate (65  $\mu$ m PDMS/DVB, 5 min extraction, 24  $^{\circ}$ C).



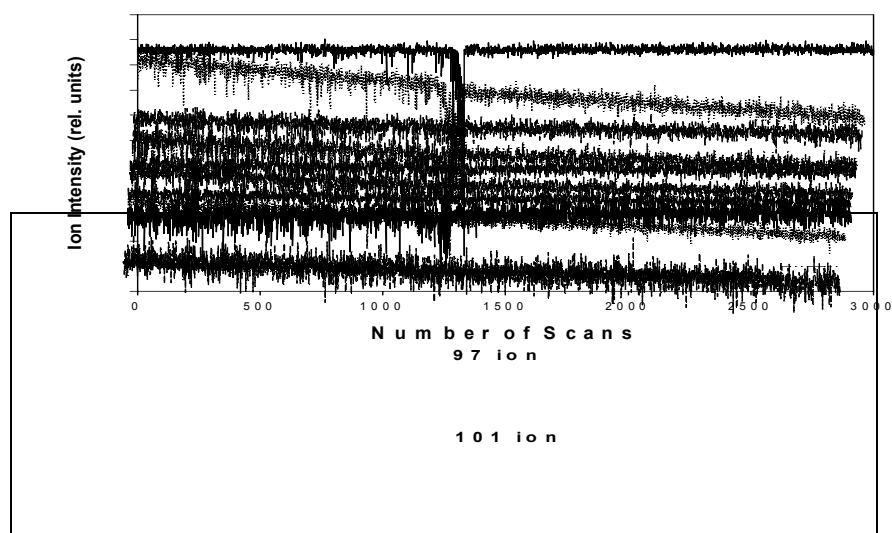
**Figure 6-4.** Headspace SPME/GC-PI-MS total ion chromatogram from analysis above neat diisopropylamine (65  $\mu$ m PDMS/DVB, 5 min extraction, 50  $^{\circ}$ C).



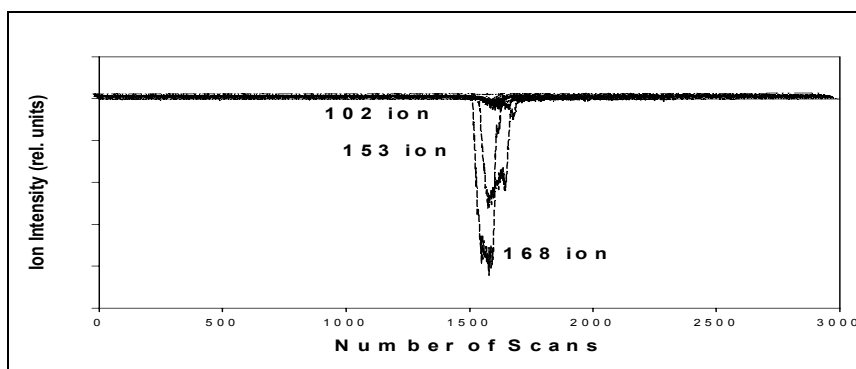
**Figure 6-5.** Headspace SPME/GC-PI-MS total ion chromatogram from analysis above neat thiodiglycol (65  $\mu$ m PDMS/DVB, 5 min extraction, 75  $^{\circ}$ C).



**Figure 6-6.** Headspace SPME/GC-PI-MS total ion chromatogram from analysis above neat thionyl chloride (65  $\mu$ m PDMS/DVB, 5 min extraction, 50  $^{\circ}$ C).



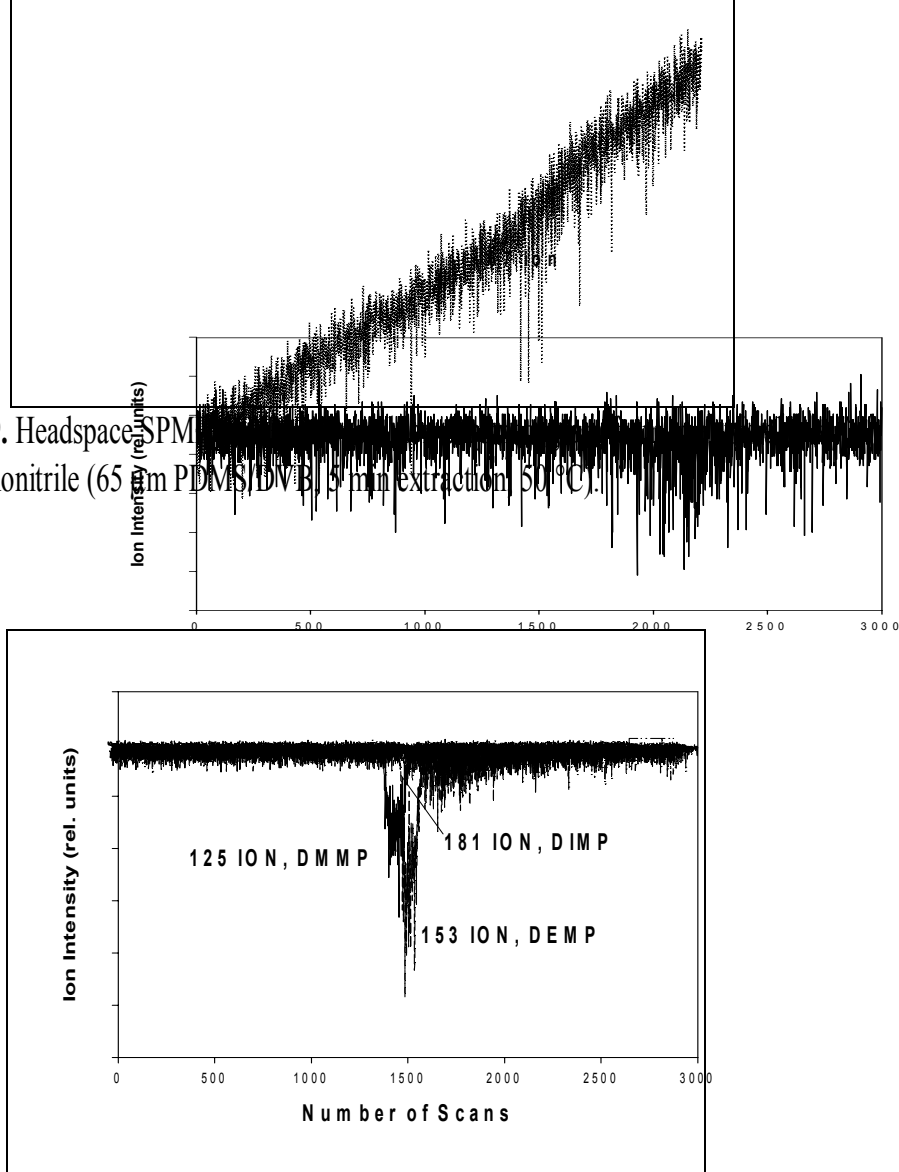
**Figure 6-7.** Headspace SPME/GC-PI-MS total ion chromatogram from analysis above neat pinacolyl alcohol (65  $\mu$ m PDMS/DVB, 5 min extraction, 50  $^{\circ}$ C).



**Figure 6-8.** Headspace SPME/GC-PI-MS total ion chromatogram from analysis above neat diethyl methyl phosphonothioate (65  $\mu$ m PDMS/DVB, 5 min extraction, 50  $^{\circ}$ C).

**Figure 6-9.** Headspace SPME

neat malononitrile (65  $\mu$ m PDMS/DVB, 5 min extraction, 50 °C).



**Figure 6-10.** Headspace SPME/GC-PI-MS total ion chromatogram from analysis above 1.0  $\mu$ L neat DMMP, DIMP, DEMP injected into a 1L Tedlar bag (65  $\mu$ m PDMS/DVB, 5 min extraction, 24 °C).

#### 4. Limitations

The limits of detection achieved as well as the inability to detect certain of these chemicals may have been due to coldspots in the transfer line or non-optimum equipment software settings. The Syagen Fieldmate<sup>TM</sup> software is currently limited in the ability to analyze data. Also, these data files are not currently exportable or viewable in any other

software, other than as shown here which was done by exporting the data to a spreadsheet. Peaks are difficult to identify due to poor ion peak resolution.

In order to do quantitative analysis on this prototype system, it was necessary to perform an initial scan, detect a particular ion of interest, then re-perform the analysis after inputting the selected ion mass. The new Syagen dual EI/PI source (as first used by Eckenrode et al [24]) will alternately scan with both detectors during the same run, allowing both soft and hard ionization and a highly selective identification of a substance.

## **5. Conclusions**

This prototype QitToF PI-MS system, mated to a flash-GC and SPME sampling, was not as sensitive as a flash-GC equipped with a quadrupole electron ionization MS (Viking). The PI source in this system has a potential for detection of specific chemicals but is most likely not well suited for mixtures of unknowns. This prototype system has potential for field application in a miniaturized version, applicable to field detection of specific chemicals, as proposed by Syagen Technology, Inc. The Syagen dual source EI/PI as discussed by Eckenrode et al. [24] will have greater overall utility than a simple PI source for sampling complex environmental samples. This benchtop prototype demonstrates the applicability of using SPME to introduce a sample via a flash-GC column for analysis on the QitToF PI-MS.

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## CHAPTER 7

### CONCLUSIONS

#### I. DISCUSSION OF RESEARCH FINDINGS

Solid phase microextraction (SPME) sampling was combined with gas chromatography-mass spectrometry (GC-MS) analysis and explored for laboratory and field sampling of complex matrices for the detection and quantification of chemical warfare agent precursors. The greatest benefit to using SPME-GC-MS methods described here is that the method allows unambiguous detection and identification of chemical warfare agent (CWA) precursors as well as common low molecular weight hydrocarbons that are commonly found as environmental contaminants.

In Chapter 3, SPME was shown to be functional with GC-MS detection for the analysis of cyanide and some common hydrocarbon contaminants in water. Sampling 0.3 to 33.4 ppm solutions of  $\text{CN}^-$  for 5.0 min at 30 °C gave a linear correlation for HCN peak area plotted against concentration. Full scan detection was possible at detection levels as low as 0.3 ppm  $\text{CN}^-$  in solution, and as low as 0.07 ppm by selected ion monitoring. The choice of 5 min extraction time, while not producing as low an apparent limit of detection as would a longer extraction time, was shown to be useful in a field setting. This method's apparent detection limit was lower than the U.S. Army's goal of 6 ppm and was close to the EPA limit of 0.2 ppm. This methodology would be useful for military and civilian chemists and first responders charged with analyzing drinking water samples in the field. The advantage displayed by this methodology over standard water analysis testing is that SPME can concentrate chemicals present in trace amounts, allowing low

limits of detection for CWA precursors as well as common hydrocarbon contaminants while standard testing only reveals the presence of selected chemicals.

In Chapter 4, SPME and fast GC-MS analysis were shown to be useful for the detection of diisopropylamine (DIPA) in the headspace above water and soil samples in a field setting, in the presence of common hydrocarbon contaminants. Detection of DIPA was performed in a standard agricultural soil (5.0 min, 30 °C, 0.72 - 3584.5 µg DIPA/g soil) and in deionized water (15.0 min, 70 °C, 0.018 - 17.9 µg/mL). Through the use of 15 min extraction and selected ion monitoring, DIPA in water was detected at levels as low as 0.009 µg/mL. This methodology is applicable to initial onsite analysis of soil and water and for onsite investigation and initial health risk assessment of potential chemical warfare agent production facilities by military and civilian first responders that are equipped with a GC-MS.

In Chapter 5, solid phase dynamic extraction (SPDE) was shown to be a novel concept that is suitable for field sampling of CWA precursors and common hydrocarbons in air samples. While this instrumentation is suitable for headspace sampling of soil and water, the manual methodology used here differs from previous research with the Chromsys commercial product in that the liquid media is not drawn up into the SPDE needle for repeated aspirations. SPDE sampling of DIPA (1 min extraction, 0.036 - 716.9 mg/m<sup>3</sup>) and dimethyl methylphosphonate (DMMP, 5 min extraction, 0.058 - 1150.0 mg/m<sup>3</sup>) in air provided linear results that achieved equivalent or lower apparent limits of detection and gave significantly larger extracted ion mass to charge peak areas than comparable SPME sampling. The SPDE displayed increased mechanical strength and better limits of detection and sensitivity compared to commercial SPME fibers.

In Chapter 6, a novel quadrupole ion trap, time-of-flight photoionization mass spectrometer (QitTof PI-MS) was shown to be functional for the detection of CWA precursors that were concentrated and introduced by a SPME fiber via an injection port and fast GC column that were added to the existing equipment. This prototype detection system, while not as sensitive as a GC-MS with electron ionization, is proof that QitTof PI-MS will work with a fast GC and SPME for detection of CWA precursors. Further testing will need to be accomplished on the next generation system to advance the concept of a truly field-portable system, especially with the addition of a dual electron ionization/photoionization source.

In summary, this body of research proved that solid phase microextraction is useful for the detection and quantitation of low levels of chemical warfare agent precursors in the presence of common volatile organic contaminants and complex matrices. In addition, electron ionization GC-MS, photoionization fast GC-MS, and electron ionization fast GC-MS, were shown to be compatible with sample concentration and introduction by SPME in both laboratory and field settings. Detection of unknown chemicals in complex matrices and complex mixtures at initial sampling and possible quantitation of analytes of interest are steps in health risk assessment. SPME-GC-MS can be a very useful tool for initial detection, and may be used for quantitation of CWA precursors in a field setting, with directly contributions to force health protection.

## **II. RECOMMENDED RESEARCH**

There are a number of areas of research that are worth further investigation. SPME methodology could be expanded to include more of a traditional industrial hygiene, health risk assessment role if further testing was performed. The additional tests

would be along the lines of those used to set the limits of detection for the Occupational Safety and Health Administration air sampling and detection methods and Environmental Protection Agency soil and water standard methods. There are a number of applications for SPME that are of great potential interest, including the helical SPME device introduced by Ciucanu [1]. This device may be useful for time weighted averaging as a personnel monitoring badge.

The Syagen QitTof PI-MS and the SPDE both need further testing and evaluation to ensure they are optimized for field use by first responders and military environmental health scientists. Further development of the Syagen software and hardware, in particular, would lead to smaller size, lower power requirements, and increased functionality while increasing the analytical power available to the field scientist.

There are several other commercially available SPDE polymers that are also worth testing for potential field use. Chromsys, Inc. has recently added a number of new polymers to their SPDE product line (Table 7-1). Many other polymers are available for use in SPDE needles upon special request from the company [2]. These other polymers will allow more selective applications, with the ability to specifically target polar and non-polar, high and low atomic weight, and high and low volatility analytes of interest.

**Table 7-1.** Chromsys, Inc. Polymers (Adapted from Chromsys [2] and Pawliszyn [3]).

<b>Chromsys Product</b>	<b>Polarity, Adsorbent/Absorbent</b>	<b>Description</b>	<b>Application</b>
PDMS	Nonpolar. Absorbent.	100% Polydimethyl Siloxane (PDMS)	Volatiles, non-polar organics (VOCs, polycyclic aromatic hydrocarbons, organochlorine pesticides).
CT 5	Nonpolar. Absorbent.	5% Phenyl Polymethylsiloxane, 95% PDMS	Semi-volatiles.
CT 1701	Bi-polar (low to mid-polarity). Unknown.	14% Cyanopropylphenyl Polysiloxane	Pesticides.
CT 225	Polar. Unknown.	50% Cyanopropylphenyl Polysiloxane	Volatiles.
Carbowax	Polar. Unknown.	Polyethylene Glycol (Wax)	Alcohols, esters & aldehydes, low molecular weight acid compounds.
PA	Polar. Absorbent.	Polyacrylate (PA)	Polar organic compounds such as triazines, organophosphorous pesticides and phenols.
CAR-PDMS	Bipolar. Absorbent + adsorbent.	10% Carboxen, 90% PDMS	VOCs, hydrocarbons.

The miniaturized flash GC-MS envisioned by Sloan [4] and under testing at the Uniformed Services University of the Health Sciences Environmental Health Sciences Laboratory will be a step forward toward a truly field portable instrument. When fully functional and tested, it will provide a powerful tool for the field analysis of potentially harmful chemicals.

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